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The Journal of

CLINICAL NUTRITION

Nov.-Dec. 1953

VOLUME 1 — NUMBER 7

AN INTERNATIONAL JOURNAL REPORTING THE PRACTICAL APPLICATION OF OUR NEWER KNOWLEDGE OF NUTRITION

UNIVERSITY OF MICHIGAN

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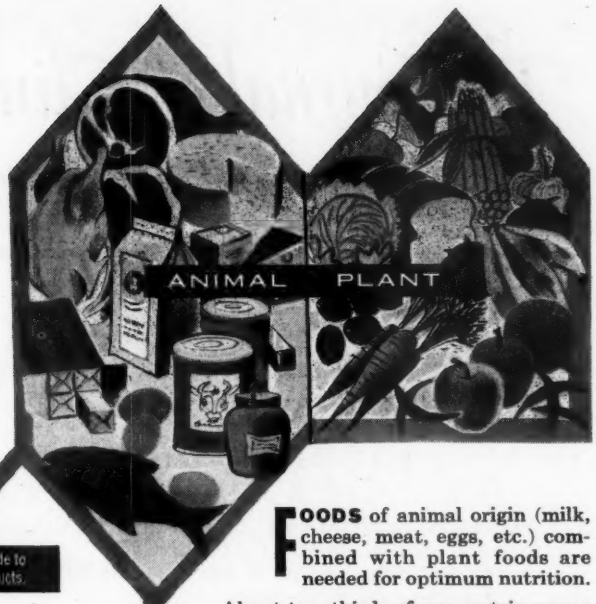

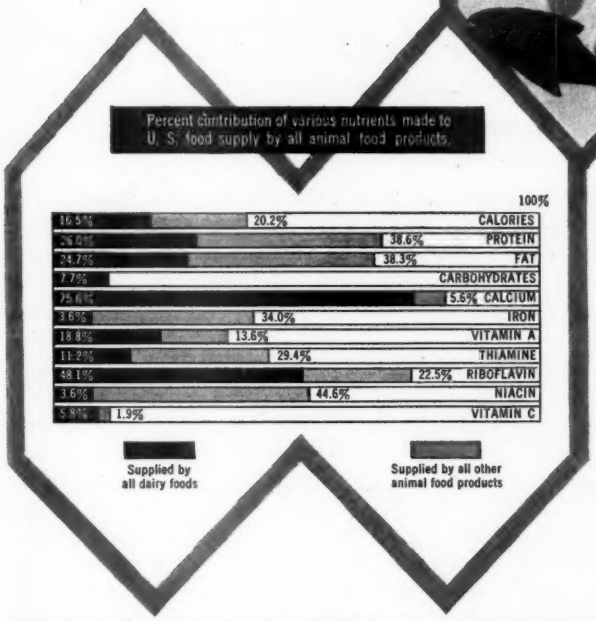

FOODS of animal origin (milk, cheese, meat, eggs, etc.) combined with plant foods are needed for optimum nutrition.

About two-thirds of our protein comes from animal foods.[1] Most animal protein has a high biological value, by virtue of its content of essential amino acids. Animal foods are also a source of vitamin B_{12}, a factor necessary for red blood cell regeneration. There is evidence that the presence of animal protein foods in the diet favors normal lipid metabolism.[2]

Four-fifths of our calcium comes from animal foods, chiefly from dairy products. Without dairy foods it is exceedingly difficult to meet the requirements for calcium. Animal foods also supply three-fourths of our available riboflavin, one-half our niacin, and one-third of our thiamine.[1] These and other vitamins are necessary for normal cellular metabolism.

Animal foods contain cholesterol, a lipid which is a normal constituent of all body cells, and which is synthesized by the body from substances derived from protein, fats, and carbohydrates. Disturbed lipid metabolism may result in deposition of cholesterol with fatty acids and protein in the inner walls of the blood vessels. This condition, atherosclerosis, is a forerunner of a number of cardiovascular diseases.[3]

Atherosclerosis is frequently associated with obesity, diabetes, and other metabolic disorders.[3,4] The cause of atherosclerosis has not been determined. Restriction of dietary cholesterol by elimination of animal foods has not been shown to be beneficial in its prevention or cure.[4]

The omission of the valuable nutrients found in these foods constitutes a nutritional risk not justified on the basis of currently available evidence.[5]

[1]Data supplied by Bureau of Human Nutrition and Home Economics, Agricultural Research Administration, U.S.D.A. (April) 1952.
[2]Okey, R., and Turner, E. Dietary protein as a lipotropic agent for cholesterol. Fed. Proc. *10*:390 (March) 1951.
[3]Gofman, J. W., and Jones, H. B. Obesity, fat metabolism and cardiovascular disease. Circulation *5*:514 (April) 1952.
[4]Keys, A. Human atherosclerosis and the diet. Circulation *5*:115 (January) 1952.
[5]Hegsted, D. M. Further comments on cholesterol. Presented before American Medical Association, Los Angeles, December 1951.

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NOVEMBER–DECEMBER, 1953 VOLUME 1, NUMBER 7

The Use of FAT SUPPLEMENTS *in the Nutrition of* CRITICALLY ILL PATIENTS

By GORDON M. MINDRUM, M.D.*

ADEQUATE nutrition is of great importance in the treatment of severe and protracted illness. The marked loss of weight and the complications of inadequate alimentation in the critically ill and convalescent patient are well known.[1–7]

The rate of metabolism is accelerated in many types of diseases. Jolliffe[8] points out that a temperature rise of 1° C. elevates the basal metabolic rate by 13 per cent. In agitated patients, there may be an additional 30 per cent increase.[8] In severe febrile illness more nitrogen is usually excreted in the urine than can be taken into the body, even when large amounts of protein are consumed. Losses of body protein as high as 500 Gm. a day have been recorded in febrile states.[8] Although there is an increased need for calories, the anorexic and critically ill patient cannot ingest an adequate amount. It is usually impossible to administer to even the most cooperative subject the required number of calories in the form of natural foods.

When the caloric input is insufficient for metabolic needs, the reserve supplies of the body are quickly exhausted.[8] If carbohydrate and fat supplies are inadequate, the body must utilize ingested and body protein as sources of energy. This use of protein, i.e., the deamination and conversion to glycogen, is a caloric-ally wasteful procedure.[9] The resultant muscle wasting and other consequences of such negative nitrogen balance have been well described in many studies.[8,10,11]

Attempts have been made to establish nitrogen balance by high caloric diets consisting mainly of carbohydrate along with moderate amounts of fat and protein. In 1909, Shaffer and Coleman[12] obtained nitrogen balance in patients with typhoid fever using a diet consisting largely of carbohydrate and ranging from 3500 to 5000 calories daily. With such a diet, mortality was lessened, notable improvement in well-being occurred, loss of weight was greatly curtailed, and convalescence accelerated. The diet, however, was bulky and difficult to administer and could not be given to the comatose patient. Since then, various other methods have been advocated as a means of supplying supplementary calories. Egg nogs, enriched milk and ice cream drinks, alcoholic beverages, interval and night feedings have been tried, and various attempts have been made to stimulate appetite. In the critically ill patient, these methods have usually been unsuccessful.

From the Department of Internal Medicine, University of Cincinnati Medical School.

* Fellow in Gastroenterology, University of Cincinnati.

TABLE I

Color, Sex, Age	Diagnosis	Status at the start of treatment	Results after high caloric diet intake
1. G. J. #290574 W. Male, 31	Acute epidural hematoma, cerebral contusion, scalp lacerations	Prolonged decerebrate rigidity with hyperventilation and hyperthermia. Deep coma. Acute tracheobronchitis. Multiple severe decubitae. Cystitis. 43-lb. weight loss in 26 days	Healing of wounds and decubitae. Infections controlled. Weight gain 13 lb. in 75 days. Stuporous
2. R. G. #289661 W. Male, 34	Crushed pelvis. Fractured left hip, left elbow and forearm, right forearm, right ankle, skull fracture, brain contusion, kidney contusion	Comatose with numerous convulsions. Multiple large decubitae. Toxic spiking fever. 51-lb. weight loss in 31 days	Decubitae healed. Fracture healing. Temperature normal. Surgery now possible on left hip. Weight gain 17 lb. in 47 days. Semicomatose
3. J. W. #262621 C. Male, 39	63% 3rd and 2nd degree burns	50-lb. weight loss in 41 days. Toxic with high fever. Infected burned surfaces. Severe emaciation. Large decubitae. Psychotic	Firm granulation tissue with good healing. Healing decubitae. Oriented. Weight gain 28 lb. in 2 months
4. W. J. #289919 W. Male, 69	BPH with retention, GU infection, prostatectomy	30-lb. weight loss. Debility. Wound dehiscence. Poor wound healing. Unco-operative	Weight gain 15 lb. Increased strength. Wound healing improved. Co-operative
5. B. F. #285441 W. Female, 21	Bilateral far advanced pulmonary tuberculosis	Weight stable for one month. Toxic. Depressed	20-lb. weight gain in 2 months Marked increased strength and well-being
6. A. S. #290503 W. Male, 48	Empyema of right lung	Toxic. Marked malnutrition. Extreme debility. Febrile. 40-lb. weight loss to 88 lb.	Weight gain 27 lb. in 49 days. Increased strength. Afebrile. Chest dry
7. C. H. #285712 C. Female, 82	Empyema. Far advanced pulmonary tuberculosis	Toxic. Extreme debility. Weight loss to 52 lb.	20-lb. weight gain. Clinical improvement. Improvement in strength, sensorium and appetite
8. A. T. #288671 C. Female, 42	Malnutrition, alcoholism, CNS lues, pneumonia	Extreme debility and malnutrition. Psychotic. Food refusal. Weight loss to 63 lb.	Weight gain 18 lb. in 36 days. Clinical improvement
9. L. B. #264163 C. Male, 66	Carcinoma of larynx	Emaciation. Weight loss to 91 lb. Febrile. Disoriented. Unco-operative	Weight gain 15 lb. in 60 days. Oriented and co-operative. Strength gain. Supplements discontinued and weight dropped 16 lb. in 20 days. Patient restarted on emulsion and gained 22 lb. in 60 days

Studies on the physiology of starvation[10,11] indicate that a severely malnourished person can tolerate a regular diet and that the most important consideration in recovery is caloric input rather than type of foodstuff or method of administration. Other studies[12] have indicated also that critically ill patients can absorb high caloric diets.

Because of their high caloric value, fat mixtures are currently being studied extensively as a means of giving calories. Black and associates[13] have investigated the importance of fat in the diet. They have demonstrated that, when diets of constant amounts of protein and calories are administered, the efficiency of energy utilization varies directly with the fat

content.[13] If the protein content of the diet is maintained constant, a negative nitrogen balance can be made positive merely by caloric supplementation.[14,15] Consequently, many groups have advocated the use of fat supplements to provide extra calories for the establishment of a positive nitrogen balance.[16–21] It has been shown that dietary fat, by virtue of its caloric properties, spares protein.[16,22] Such diets can be tolerated in from 60 to 80 per cent of cases, and weight gain can be achieved.[9,20,21] This communication presents data observed during the administration of high caloric, high fat diets to 9 patients, each exhibiting symptoms of protein depletion.

Methods

Studies were made on nine critically ill selected patients from the medical and surgical services of the Cincinnati General Hospital. In Table I are listed pertinent data concerning diagnosis, condition at time of institution of dietotherapy, and results of treatment. All patients showed striking weight loss, progressive debility, a febrile course, and complications such as decubitae and mental changes. Observations were made during a control period when the patient was offered the regular hospital diet or a variation, and during a treatment period when supplements of fat mixtures were added to the regular diet. The average intake in the control periods was generally less than 2000 calories per day, and during the treatment period 4000 to 5000 calories per day.* The duration of the treatment periods varied from 30 to 120 days. Therapy directed toward the primary disorder was the same in both periods. In no case was blood or plasma given after the institution of the high calorie intake.

The dietary supplements given consisted mainly of fat emulsions administered by mouth or by stomach tube. The composition of the mixtures was as follows:

Edible Oil—peanut, coconut, or salad oil used in percentages from 20 to 50% by volume†
Carbohydrate—sucrose, 10 to 15% by weight
Emulsifying Agent—Sorlate, 2% by volume‡
Flavor—vanilla extract, peppermint, chocolate, coffee
Protein—powdered skim milk up to 23% by weight
Water—enough to make 100 cc.

One type of mixture found to be well tolerated consisted of 50 per cent oil, 12 per cent sucrose, 2 per cent emulsifying agent, vanilla flavor, and water. Such a mixture furnishes *5.1 calories per cc.*§ It can be further fortified by adding skim milk powder. Twenty-three Gm. of skim milk powder added to the mixture does not greatly change the volume, but adds much to palatability, protein content, and calories. Analysis of this fat mixture for nitrogen, sodium, and potassium is given in Table II.‖ The mixture can be easily prepared with a Waring blendor or a colloid mill. It is adequately stable for practical use and can be mixed with water, milk, fruit juice, or standard tube feedings. Such mixtures have remained stable in the ward refrigerators for one to two weeks. If the mixture is used in a matter of a few hours, it can be prepared with a malted milk mixer.

TABLE II

Analysis of Fat Mixture: 50% oil, 12% sucrose, 2% emulsifying agent. With and without skim milk powder

	Nitrogen	Sodium	Potassium
	Gm. per 100 cc.	*Mg. per 100 cc.*	*Mg. per 100 cc.*
Without skim milk	0	3	3
With skim milk, 23% by wt.	5.13	96	336

During diet therapy there was need for continuous observation and encouragement over the long period of treatment. Fat emulsions were made according to the individual patient's tolerance and taste. The flavor was changed periodically, employing such ingredients as vanilla, chocolate, coffee, peppermint, etc. Fat supplements and diet were adjusted day by day to the tolerance of the patient. For example, on the day of each burn dressing,

* All calorie counts for this study were accomplished by the Department of Dietetics of the Cincinnati General Hospital.

† Edible oil was donated by Eli Lilly & Company.

‡ Sorlate was donated by Abbott Laboratories.

§ This mixture was donated by Schenley Laboratories.

‖ Analyses were done by Harvey C. Knowles, M.D., Assistant Professor of Medicine, University of Cincinnati.

patient No. 3 was able to take only one-third of his usual diet and supplement. In particularly intolerant or unco-operative patients it was necessary to give the emulsion by slow drip through a polyethylene gastric tube. The addition of Kaopectate® was of aid to some patients who developed diarrhea.

The fat supplement was given as a medication, usually a half hour after meals. The amounts administered were increased every other day. Thirty cc. were given three times a day for two days, 60 cc. at a time for two days, and finally 100 cc. after each meal. The importance of eating all meals was stressed repeatedly. Night feedings were instituted in several cases, and the fat mixture was administered after these feedings as well. Total caloric input in each case exceeded 4000 calories a day.

Results

The courses of the patients are depicted in Table I. In all nine cases there was improvement in both nutrition and general status, increase in general strength, sense of well-being and morale. Wounds healed more rapidly, and decubitae, previously resistant to any therapy, decreased in size or disappeared. Temperatures previously elevated returned to normal.

In Figures 1, 2, and 3 are charted the courses of three patients. These patients are representative of the entire group.

No ill effects from the fat emulsion were noted in this series. Gastroenteric complaints were minimal. Although there was some variation in tolerance to the mixture, all of the group were able to ingest at least 100 cc. three times a day. One patient received 600 cc. a day for 90 days without complaint. Patient **B. F.** developed nausea in the middle of her treatment period. However, decreasing the amount of emulsion by 50 per cent resulted in a gradual return to the original tolerance. It should be noted that concomitantly she was receiving 12 Gm. of para amino salycilic acid a day, which may well have contributed to the nausea. Patient **W. J.** developed mild diarrhea at the termination of his treatment period. The simultaneous administration of tetracycline (Terramycin®) may have been accountable.

Case Reports

Case 1

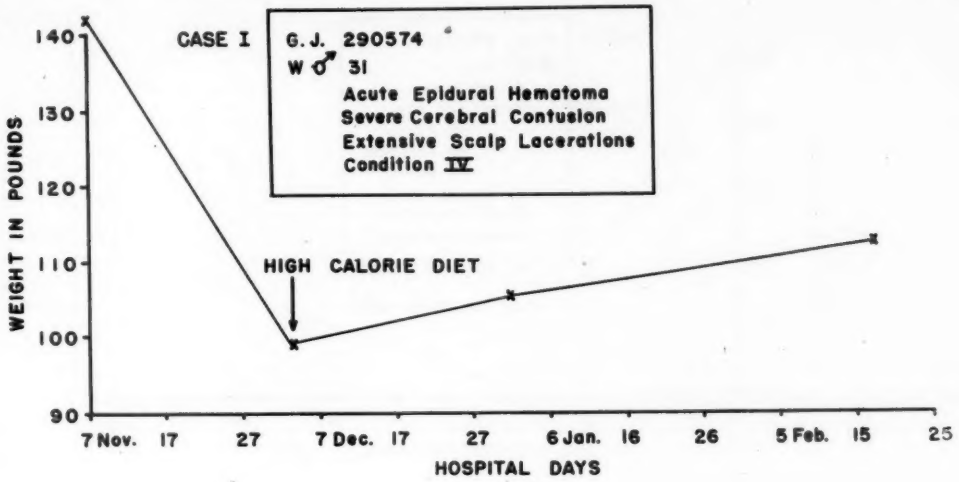
G. J. (CGH #290574), a 31-year-old white student, was admitted November 7, 1952, following an automobile accident, with an acute epidural hematoma, cerebral contusion, and severe scalp lacerations. There were prolonged episodes of decerebrate rigidity with hyperventilation and hyperthermia. He was in a state of deep coma. Complications included multiple decubitae, purulent tracheobronchitis, cystitis, and infected scalp wounds. His course was downhill and was accompanied by fever and convulsions. He received the regular hospital tube feeding which contained an average of 1875 calories per day. His admission weight of 142 lb. had declined to 99 lb. on December 3. At this point fat supplements were added to his diet and there was progressive clinical improvement thereafter. On January 1, his weight was 105 lb. and on February 18, 112 lb. The decubitae and scalp wounds healed, and his temperature returned to normal. He remains stuporous but can speak and will respond to simple commands. The nursing demands have been greatly reduced.

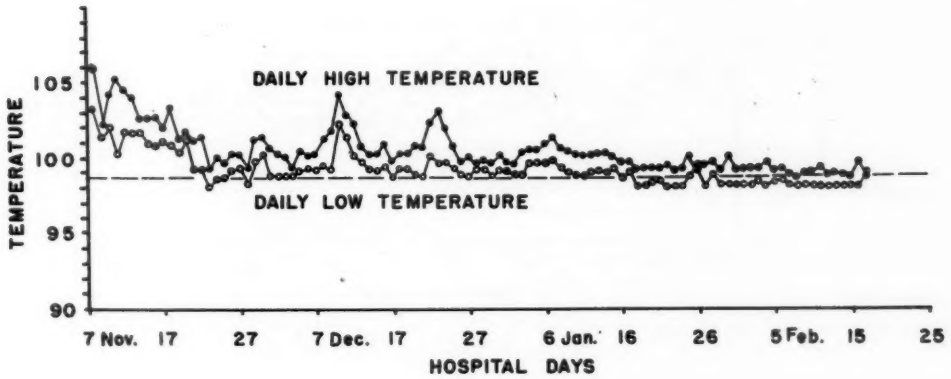
Case 2

R. G. (CGH #289661), a 34-year-old white engineer, was admitted on September 28, 1952, following an automobile accident. He was in shock from multiple fractures involving the skull, pelvis, and all extremities. Movement of the patient was impossible because of the diffuse injuries. Numerous generalized convulsions occurred. By October 27, there were multiple large decubitae. Coma persisted throughout the entire hospitalization. He ran a high spiking temperature. Despite plasma and blood transfusion and debridement of the decubitae, the course of the patient was downhill. Dietary intake by tube averaged 1875 calories per day. On October 31 his condition was critical. The admission weight of 152 lb. had decreased to 101 lb. At this point fat supplements were added to his diet, providing a daily caloric intake exceeding 4000 calories. Improvement was noted within two weeks. Decubitae began to heal, and his temperature returned to normal. On November 17, it was possible to pin his left hip. By December 18, his weight had increased to 118 lb., and all decubitae had healed except one. He was then transferred to another hospital where his course has continued satisfactorily. All fractures have healed except that of his left elbow which had been completely fragmented.

Case 3

J. W. (CGH #262621), a 39-year-old colored male mechanic, was admitted on August 22, 1952, with


CASE I
G. J. 290574
W ♂ 31
Acute Epidural Hematoma
Severe Cerebral Contusion
Extensive Scalp Lacerations
Condition IV
HIGH CALORIE DIET
WEIGHT IN POUNDS
140
130
120
110
100
90
7 Nov. 17 27 7 Dec. 17 27 6 Jan. 16 26 5 Feb. 15 25
HOSPITAL DAYS


DAILY HIGH TEMPERATURE
DAILY LOW TEMPERATURE
TEMPERATURE
105
100
95
90
7 Nov. 17 27 7 Dec. 17 27 6 Jan. 16 26 5 Feb. 15 25
HOSPITAL DAYS

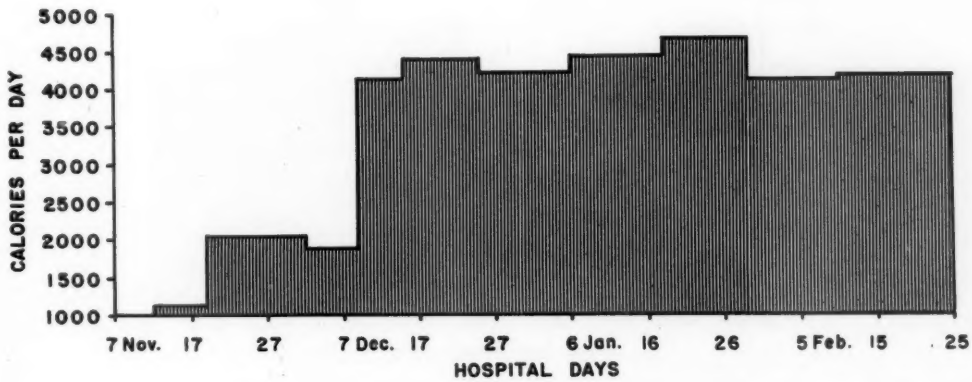
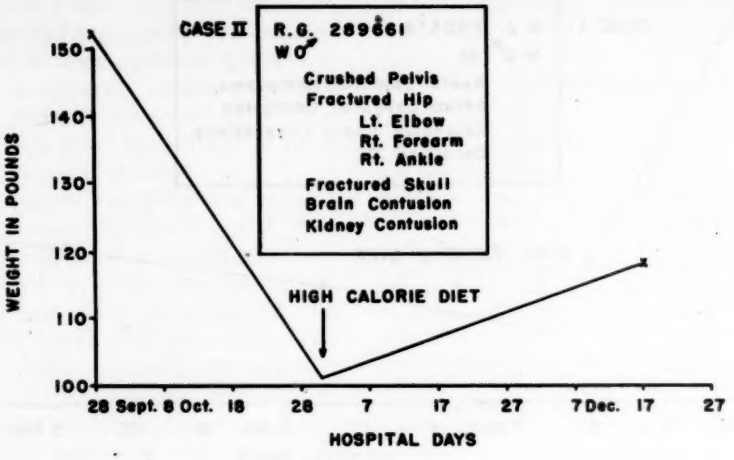
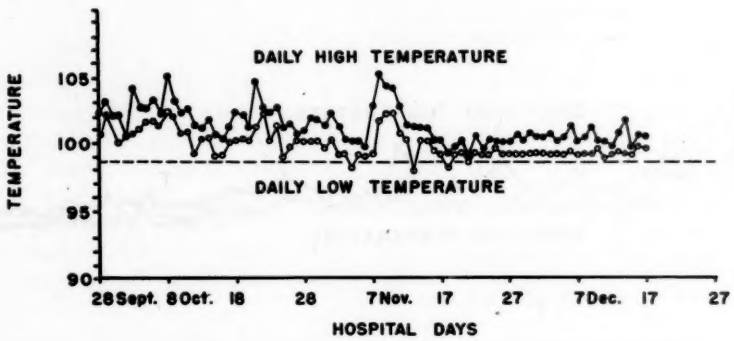

CALORIES PER DAY
5000
4500
4000
3500
3000
2500
2000
1500
1000
7 Nov. 17 27 7 Dec. 17 27 6 Jan. 16 26 5 Feb. 15 25
HOSPITAL DAYS

Figure 1


CASE II
R.G. 289661
W ♂
Crushed Pelvis
Fractured Hip
Lt. Elbow
Rt. Forearm
Rt. Ankle
Fractured Skull
Brain Contusion
Kidney Contusion
HIGH CALORIE DIET
WEIGHT IN POUNDS
150
140
130
120
110
100
28 Sept. 8 Oct. 18 28 7 17 27 7 Dec. 17 27
HOSPITAL DAYS


DAILY HIGH TEMPERATURE
DAILY LOW TEMPERATURE
TEMPERATURE
105
100
95
90
28 Sept. 8 Oct. 18 28 7 Nov. 17 27 7 Dec. 17 27
HOSPITAL DAYS

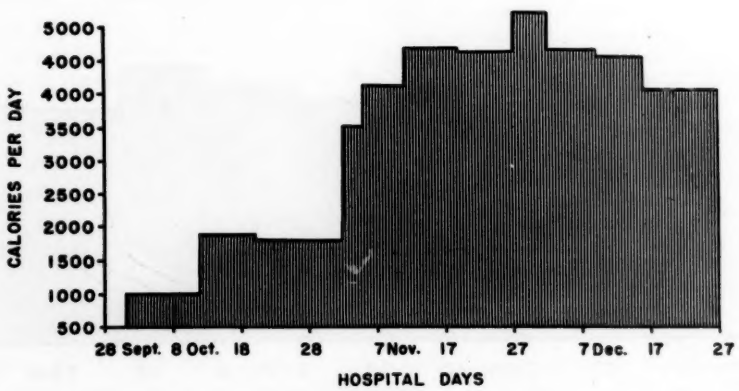
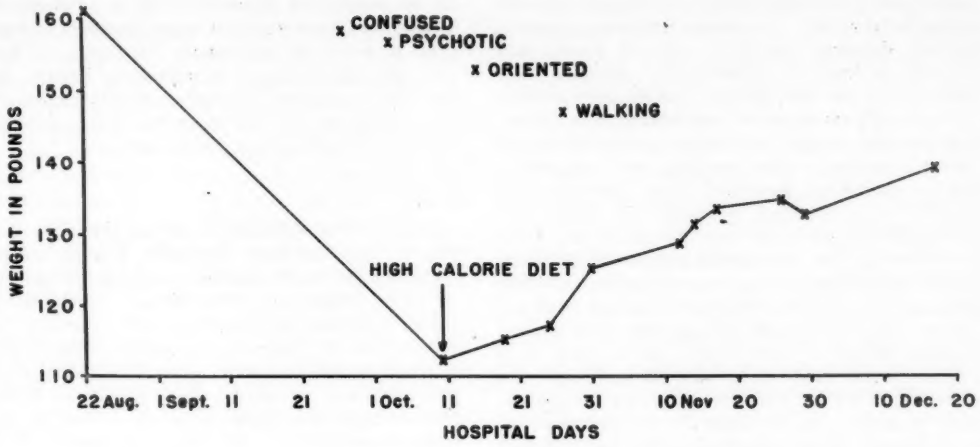
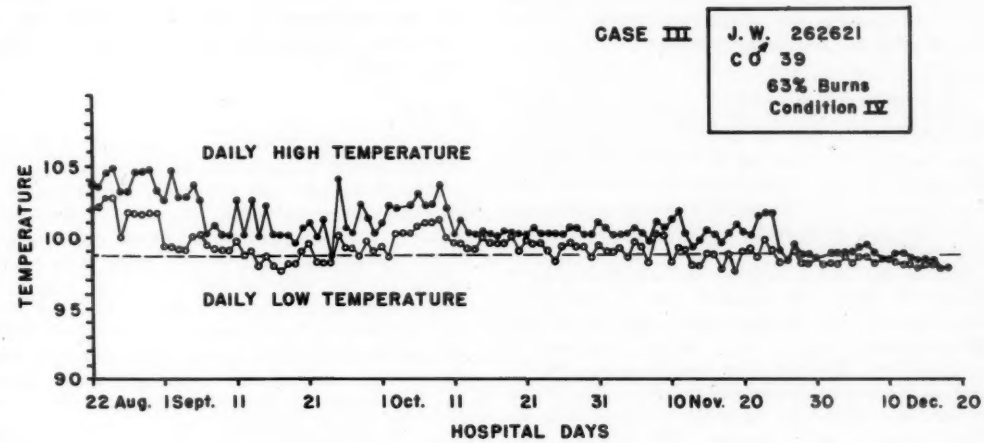

CALORIES PER DAY
5000
4000
4000
3500
3000
2500
2000
1500
1000
500
28 Sept. 8 Oct. 18 28 7 Nov. 17 27 7 Dec. 17 27
HOSPITAL DAYS

Figure 2


CONFUSED
PSYCHOTIC
ORIENTED
WALKING
HIGH CALORIE DIET
WEIGHT IN POUNDS
160
150
140
130
120
110
22 Aug. 1 Sept. 11 21 1 Oct. 11 21 31 10 Nov 20 30 10 Dec. 20
HOSPITAL DAYS


CASE III
J. W. 262621
C ♂ 39
63% Burns
Condition IV
DAILY HIGH TEMPERATURE
DAILY LOW TEMPERATURE
TEMPERATURE
105
100
95
90
22 Aug. 1 Sept. 11 21 1 Oct. 11 21 31 10 Nov. 20 30 10 Dec. 20
HOSPITAL DAYS

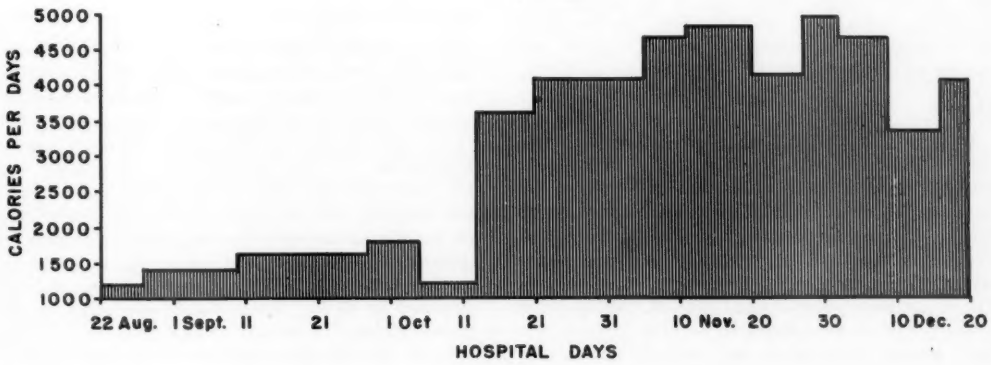

CALORIES PER DAYS
5000
4500
4000
3500
3000
2500
2000
1500
1000
22 Aug. 1 Sept. 11 21 1 Oct 11 21 31 10 Nov. 20 30 10 Dec. 20
HOSPITAL DAYS

Figure 3

second and third degree burns involving 63 per cent of the body surface. Treatment included antibiotics, pressure dressings, and 41½ units of plasma and blood given during the 15 days after admission. The patient took oral feedings well, but his average daily caloric intake amounted to only 1800 calories. There was marked weight loss, fever, and infection of burned surfaces. Skin grafting was impossible. Severe emaciation developed, large decubitae appeared, and he became psychotic. On October 9, his weight had declined from 162 lb. on admission to 112 lb. At this point fat supplements were added to his diet, giving a daily caloric intake exceeding 4000 calories. Within two weeks improvement occurred. There was weight gain, healing of the burned surfaces, decline of temperature, and a return to a normal mental state. On October 28, his weight had increased to 124 lb., and it was possible for the patient to walk. On November 27, he was about to be discharged, weighing 134½ lb., when he developed homologous serum jaundice. However, he continued to gain weight up to 139 lb. on December 20, at which time he was discharged. Further follow-up revealed an uneventful recovery.

Case 4

W. J. (CGH #289919), a 69-year-old white farmer, was admitted on October 25, 1952, with benign prostatic hypertrophy resulting in urinary retention and infection. He had lost 40 lb. in the six months prior to admission. On November 4, a suprapubic prostatectomy was performed. Moderate bleeding, which occurred at the time of surgery and during the following two weeks, required the administration of 6 units of blood. On November 13, wound disruption occurred, and surgical repair was carried out. Wound healing was very slow. He was weak and unco-operative. His weight on admission was 140 lb., and on November 18 was 110 lb. At this point the patient was started on fat supplements, so that his daily caloric intake exceeded 4000 calories. Previously he had eaten the regular hospital diet, which contained an average of 1625 calories daily. There was marked general improvement in strength, co-operation, and rate of wound healing. On December 3, his weight had increased to 125 lb., and he was discharged home.

Case 5

B. F. (CGH #285441), a 21-year-old white housewife, was admitted May 8 with active tuberculosis. Physical examination revealed marked emaciation and toxicity. Roentgenography showed far advanced bilateral pulmonary tuberculosis with cavitation. Treatment consisted of streptomycin, para amino salycilic acid and a high protein diet. Her weight of 117 lb. remained constant until June 21. At this point fat supplements were added to her diet to produce a daily intake in excess of 4000 calories. Previously, her daily intake had been 1675 calories. By August 12, her weight had increased to 139 lb. Toxicity decreased, and there was great improvement in strength, sense of well-being and morale. Repeat x-ray, however, showed no change in pulmonary lesions. She was then transferred to another hospital, where the fat mixture was not administered. There had been no further weight gain a month later.

Case 6

A. S. (CGH #290503), a 48-year-old white male laborer, was admitted November 3 with massive empyema due to an anerobic streptococcus and bacteriodes. Emaciation was striking. Treatment included penicillin, streptomycin, and proteolytic enzymes. On November 9, the patient weighed 88½ lb. Fat supplements were added to his diet, which had previously averaged only 1250 calories a day. Improvement was noted while on a diet of over 4000 calories per day. His weight increased to 99 lb. on November 22 and to 115 lb. on December 28. The empyema had resolved completely by December 22. Since discharge, the patient has been seen in the Outpatient Clinic and has continued to gain in weight and strength.

Case 7

C. H. (CGH #285712), an 82-year-old retired colored female teacher, was admitted on May 15, 1952, with far advanced pulmonary tuberculosis and empyema. She was acutely ill, and emaciation was striking. Antibiotic treatment included penicillin and streptomycin. She received an average daily caloric intake of only 1300 calories. From an admission weight of 80 lb. there was a decline to 52 lb. by June 22. At this point fat supplements were added to her diet so that her daily caloric input exceeded 4000 calories. On July 14, she weighed 74½ lb. There was improvement in sensorium, strength, and appetite. Her fever decreased. The pulmonary lesions showed little change. Subsequently, she was transferred to another hospital.

Case 8

A. T. (CGH #288671), a 42-year-old colored housewife, was admitted August 28, 1952, with pneumonia, central nervous system syphilis, chronic alcoholism, multiple vitamin deficiencies, and severe malnutrition. Her weight stabilized at 67 lb. while eating the regular hospital diet of 1600 calories a day. The patient was very unco-operative and, at times, psychotic. Food was often refused. On September 15 she was started on the regular hospital tube feeding mixture plus fat supplements which provided a daily caloric intake exceeding 4000 calories. By October 21 her weight had increased to 85 lb. There was improvement in her general status; she became co-operative and was able to walk. She was discharged to the Outpatient Clinic and has done well.

Case 9

L. B. (CGH #264163), a 66-year-old colored male laborer, was admitted on November 28, 1952, with carcinoma of the larynx. Emaciation was marked. A laryngectomy was carried out on December 12. His weight decreased from 94½ lb. on December 1 to 91 lb. on December 30. His course was downhill and was characterized by weakness, fever, and disorientation. On December 30 he was started on tube feedings with supplemental fat which provided a daily caloric intake exceeding 4000 calories. On January 30, his weight was 102 lb., and there was improvement in strength, sense of well-being, and mental state. On March 1, his weight was 105½ lb., and additional surgery was accomplished. Following surgery, the high caloric supplement was discontinued, and weight dropped rapidly to 89 lb. on March 15. Supplements were again started and, although diarrhea did occur, weight increased to 111½ lb. on May 18.

Discussion

The aforementioned observations clearly show that the use of fat supplements to provide high caloric intake is of value in the management of malnutrition and its complications occurring during protracted illness. In each case, general improvement coincided with the administration of these supplements. All patients showed weight gain, increased resistance to infection, decrease in fever, and marked improvement in strength and morale. Of particular interest was the effect of added calories upon the rate of wound healing. Decubitae, previously resistant to any therapy, decreased in size and healed.

Fat supplements should be used in any chronic disease state wherein there is a negative nitrogen balance or failure to gain weight. In recent years, considerable emphasis has been placed upon recovery and rehabilitation. Through the use of new antibiotics, better surgical techniques, and improved knowledge of fluid and electrolyte balance, patients are being salvaged from illnesses and trauma which only a few years ago would have been fatal. However, following the acute phase, the physician is faced with problems of decubitae, hypoproteinemia, decreased resistance to infection, muscle wasting, and a host of other difficulties. In the cases presented above, fat supplements were administered only after these complications had developed. Little attention has been paid to the prevention of these sequelae, probably because, at the onset of disease, all efforts are directed toward the acute phase, and because many patients now unexpectedly survive. It would seem logical to use fat supplements at an earlier date to assist in prevention of troublesome sequelae, as well as to hasten the recovery period.

In the management of chronic wasting illness, such as far advanced tuberculosis or carcinomatosis, the supplements are valuable in that they foster a sense of well-being. If a patient can gain weight, his morale is usually improved. In addition, patients with conditions such as esophageal stenosis and post-radiation anorexia have been benefited by the fat mixture.

Although the selected patients mentioned above tolerated the mixture well, several other subjects refused to take the emulsion. Furthermore, in a group of nurses, who were attempting to gain weight, various side reactions such as anorexia, nausea, and diarrhea were noted which caused 30 per cent of the group to discontinue the diet.

Theoretical contraindications to the use of fat emulsions include gastric retention, stones in the biliary system, pancreatic insufficiency, and extensive enteric disorders associated with impaired fat absorption. Although the presence of liver disease has not been found to be a contraindication, fat supplements should be administered with caution in such instances. Fat emulsions have been given to diabetics, and no problems have resulted in regard to control or ketosis.

The fat emulsions can be prepared easily and economically in any hospital or can be obtained commercially. In our experience commercial products have been very convenient for outpatient treatment.

Summary

Supplemental calories were administered in the form of fat emulsions to nine critically ill patients who exhibited evidence of protein depletion.

In all nine cases marked improvement occurred as shown by sense of well-being, weight gain, increased resistance to infection, and accelerated rate of wound healing.

The importance of adequate caloric intake is stressed in the treatment of acute and chronic illness.

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RESUMEN

El uso de suplementos de grasa en la nutrición de pacientes críticamente enfermos

Se administraron calorías suplementarias en forma de emulsiones grasosas a nueve pacientes críticamente enfermos que presentaban evidencia de depleción proteínica.

En todos los nueve casos se observó una marcada mejoría demostrada por un sentido de bienestar, ganancia de peso, incremento en la resistencia a las infecciones y aceleración en el período de curación de las heridas.

La importancia de la ingestión adecuada de calorías es marcada en el tratamiento de enfermedades tanto agudas como crónicas.

THE WORLD BERIBERI PROBLEM TODAY

By ROBERT R. WILLIAMS, SC.D.*

BERIBERI is an ancient disease, being recognized in the medical writings of China as early as 2697 B.C. and mentioned repeatedly throughout the Christian era. Its importance as a practical health problem was recognized in many countries of Asia during the later 1800's. It became a number one health problem in Java, Malaya, Japan, and the Philippines during the first two decades of this century. At that time the literature of tropical medicine contained many reports of serious incidences of the disease, especially in jails, hospitals, military forces, and labor camps, where the diet was liable to be unvaried and consist largely of white rice.

In the Western world, beriberi in forthright form has always been of sporadic occurrence, and high incidence has been limited to isolated areas or groups of people living on a cheap and monotonous diet. Thus, railway construction parties in Brazil in 1900–1915 experienced disastrous epidemics of beriberi because, unlike the general population, they were living on a monotonous starchy diet provided by commissaries. The same experience is recorded on ships to the extent that ship's beriberi was once regarded as a specialized occupational disease. All the major seaports of the United States have at one time or another reported occasional cases of severe beriberi among sailors entering their harbors from distant ports. The early years of the century also witnessed beriberi in epidemic proportions in Newfoundland and Laborador. In the two World Wars beriberi became prevalent and destructive in various military and civilian prison camps or in areas under seige.

The nature of the occurrence of the disease, especially in the earlier decades of this century, had much to do with the revelation of beriberi as a deficiency disease. Excellent reviews of this earlier history are found elsewhere.[1,2] In modern times, beriberi in the West has become of relatively rare occurrence except in forms so mild as not to be easily recognized. Some subclinical beriberi can still be found among all populations where the consumption of white flour or rice is moderately high. It has been eliminated generally in the United States and its possessions by rising standards of living, and especially by the enrichment of white cereal products with thiamine, in addition to riboflavin, niacin, and iron. Thiamine deficiency is now rare in the United States, even among alcoholics.

Asia, however, still presents a contrast to the West in this regard, especially the rice-eating areas of East and Southeast Asia. The Middle East presumably occupies an intermediate position. However, it must be frankly stated that few of the countries in which beriberi is still somewhat prevalent possess significant statistics. In none is the incidence of beriberi known. Only in Japan[3] and the Philippines[4] are significant statistics of mortality from beriberi available. This should not be considered surprising, as all principal causes of death are equally vaguely known. Beriberi in adults is usually not an acute and highly fatal disease. Millions doubtless live for years in a partially deficient state. It is probable that 10 per cent of the population of rice-eating Asia could be shown to exhibit mild symptoms of the disease. This is especially true of women of child-bearing age. Experi-

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ence shows that morbidity must exceed mortality 100 fold. It is this heavy drain on productive health that constitutes beriberi's greatest injury to Asian populations.

Partly, at least, in consequence of the chronically ill-fed condition of the mothers, infantile mortality is extremely high in the larger part of rice-eating Asia. Lucius Nicholls, a man of wide experience in tropical nutrition, has said[5] "It appears that infantile beriberi is the only serious form of malnutrition which occurs in breast-fed infants receiving the mother's milk in adequate amounts. The disease usually occurs after the second month of life. About 50 per cent of the mothers show signs of beriberi to various degrees." In infants, the untreated disease is quickly fatal. As Nicholls says, "When there is aphonia, edema, and convulsions the diagnosis is simple, but in many cases the first two are absent, and the infant passes into convulsions with no other sign and may die with acute cardiac enlargement."

When, as is true throughout Southeast Asia with very limited exceptions, 200 to 400 infants out of every 1000 live births succumb within the first year of life, no one reliably notes the cause of death. Multiple causes may indeed be present but judging from Philippine experience it would not be surprising if one-half to two-thirds of this enormous infant mortality is due to beriberi. It is inevitable that in those Asian countries where the crowding populations constantly threaten the exhaustion of the food supply, high infant death rates are often accepted philosophically by public officials as an act of Providence to keep total populations within bounds.

The two Asian countries which have long maintained records of mortality from beriberi are the Philippines and Japan. In Japan, deaths attributed to beriberi ranged from about 10 per 100,000 in 1911 to 44 per 100,000 in 1923.[3] The rate remained high, though variable, from 1900 to 1930, after which a decline set in—due in part to the introduction of "germ rice," that is, rice retaining a part of the germ. This was further accentuated during the war years, when removal of bran in excess of 5 per cent of the weight of the rice was prohibited by government, partly as a means of maintaining adequate caloric intake for the population. This was relatively easily accomplished in Japan, where, because of general electrification, rice mills are present in every neighborhood or community. These mills were made the government rice rationing centers. The death rate from beriberi fell to 6 per 100,000 in 1943. Some rise has been observed since the close of the war in view of less strict enforcement of regulations.

Table I, taken from Philippine government reports, is indicative of the prevalence of beriberi. Deaths from beriberi have greatly declined in Manila, due in part to better feeding, but mainly to better medical care, including the distribution of rice bran extract through dispensaries and the availability of synthetic thiamine for treatment of the sick. In the provinces, however, these measures have been less generally available and no consistent decline is discernible. There are, of course, considerable fluctuations in death rates in the data for the individual provinces. Largely, these reflect actual variations in the food supply as affected by crop shortages or surpluses. The data, especially of the earlier years, are influenced by uncertain diagnoses and by varying zeal of local health officials. Infant deaths have frequently been distinguished in the official statistics from those of adults. In general, it may be said that two-thirds to three-fourths of the total deaths are those of infants.

In the remaining countries of Asia, few statistics are available. In India, the widespread use of parboiled rice which conserves in the milled grain a substantial fraction of the thiamine from the bran undoubtedly is a major preventive of beriberi, but there are areas and groups of people who use only white rice. White rice is also the staple food for Burma, Siam, Malaya, South China, and the coastal regions of Indo-China. The general character of the dietaries is not grossly different from that of the Philippines. A reasonable presumption exists of the extensive existence of beriberi in these areas. Outbreaks of beriberi are still periodically reported, as in Chiengmai in 1951, and the infant death rate continues to

TABLE I

Death Rates from Beriberi per 100,000 of Population in Manila and the Philippines (1910–1950)

Year	Manila	Philippines	Year	Manila	Philippines
1910	577	70	1930	72	159
1911	523	50	1931	42	141
1912	409	63	1932	46	121
1913	265	66	1933	41	129
1914	314	80	1934	24	146
1915	322	87	1935	68	131
1916	248	135	1936	64	97
1917	144	131	1937	53	108
1918	202	135	1938	72	108
1919	114	131	1939	79	117
1920	190	135	1940	70	112
1921	239	157	1941	No records during	
1922	216	154	1942	enemy occupation	
1923	230	164	1943	of the country in	
1924	195	166	1944	the second World	
1925	188	163	1945	War	
1926	138	154	1946	87	145
1927	72	134	1947	84	139
1928	89	129	1948	96	140
1929	128	152	1949	53	122
			1950	14	116

* Figures supplied by the Bureau of Health, Manila. In working out the mortality rates, the deaths from adult and infantile beriberi have been pooled.

be uniformly high except in parts of Malaya.

In interior Indo-China and in Indonesia, the incidence of beriberi is much reduced, as compared with earlier years, by the use of rice which has been incompletely milled either in local small mills or by hand-pounding in the homes. No doubt there are similar limited areas of little industrial development in almost all Asian countries where primitive methods of rice preparation still prevail. These still serve as a protective mechanism, because a part of the bran or germ is retained. However, in the areas of intensive rice cultivation the mills are large and thorough in operation and the rice is white. This is true of the mills of Bangkok, Rangoon, and Saigon which, for a generation, have been the sole great export centers. From them all great Asian cities draw some substantial part of their rice supply, especially in periods after exhaustion of the nearby harvests. As the industrialization of the East proceeds, there will be more and more white rice, for complete removal of the bran is almost essential for the prevention of rancidity and insect damage during long periods of transport and storage.

Clearly, the proper approach to beriberi must be by preventive measures. The mere observation of incidence of beriberi in a population costs many times more than to prevent it by dietary supplement. The preferred routes of preventive procedure are use of (1) undermilled rice, (2) parboiled rice, or (3) fortified rice. Any of these measures requires rigorous control of the nutritional quality of the rice supply through frequent inspection by government agencies of mills, shops, and imports. The enforcement of such measures will often be defeated by a popular distaste for the variety of rice prescribed. In general, white rice eaters do not like brown or parboiled rice but do accept fortified rice since its taste and appearance are not modified. Hence, artificially fortified white rice has a distinct advantage. However, it costs 1 to 2 per cent more than ordinary white rice, and wherever free competition of the two is permitted, the latter will drive out the former. Hence the sale of ordinary white rice must be prohibited or penalized if any of the three foregoing methods is to succeed.

A large-scale trial of fortified (enriched)

rice in Bataan, Philippines[6] has demonstrated its acceptability and efficacy. Through its introduction beriberi mortality dropped to unprecedented levels in Bataan. Indeed, for many months no deaths occurred where 100 to 200 deaths per year had previously been reported. These results were confirmed by clinical surveys of 12,000 persons showing a great decline in incidence of symptoms, and also by biochemical studies[7] demonstrating substantial increases in thiamine and hemoglobin in the blood.

With governmental assistance, the practice of rice enrichment is progressively being extended throughout the rice bowl area of Luzon, with the eventual aim of its exclusive use throughout the Islands. The practical problems of control and enforcement are now being studied under the rigorous test of practical experience. There is good ground for hope that within a few years beriberi will be eradicated from the Philippines, where it has long rated as second only to tuberculosis as a cause of death.

Other Asian nations will no doubt await the result with interest and be stimulated, at least to some extent, to reappraise the prevalence of beriberi among their own peoples. Enrichment with synthetic vitamins may well continue to meet with considerable resistance in all dollar-short countries, until such time as vitamins can be manufactured economically within their own borders. Control of degree of milling or introduction of parboiling may find support as more consistent with self-sustaining economics. Rigorous control of the nutritional quality of rice will be equally necessary whichever method is chosen.

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Publicity and Health

"There was a time when a person considered himself well if his senses or mind were not disturbed by stimuli coming from within himself, and rarely was he so disturbed until his attention was distracted from his interest or job in life. . .

"The citizen of today is taught daily of the dangers that threaten his body. Whether he feels unpleasant sensations or not, he is trained to fear the lurking disease. The obvious result is that people find their attention diverted from their purpose in life and directed to the state of their bodies. Their minds are developing internal radar machines to detect the slightest strange shadows within their personal orbits. When our young man of today grows old, his stiffening joints and his winter cough will lead him to seek a full investigation to see if any of the measurable functions of his body depart from an established norm. He himself will become his greatest interest. . . "

—W. J. Saxton in an Address to the Queensland Branch of the British Medical Association. *The Medical Journal of Australia* II (15): 558, 1953.

On PHYSICAL STIGMATA *Ascribed to* VITAMIN A *and* ASCORBIC ACID DEFICIENCIES

By C. A. NEWHALL, M.D.,* SUSAN B. MERROW, M.ED.,† ANN B. DURBROW,‡ M. P. LAMDEN, PH.D.,** and H. B. PIERCE, PH.D.††

JOLLIFFE, Tisdall and Cannon state, "Probably the first description of undoubted scurvy was that of DeJoinville, who accompanied the Crusaders in the thirteenth century."[1] These authors note that the first complete descriptions of the characteristic dermatoses of vitamin deficiency were published by Frazier and Hu in 1931, Lowenthal in 1933, and Nicholls in 1938.[2] Many studies have been and are being conducted in an effort to obtain more exact information concerning the specificity of certain tissue abnormalities and their relationships to blood constituent levels and nutrient intakes.[3-7]

Although recent information and improved techniques have been applied in current investigations, there is a lack of agreement among clinicians in judging the nutritional status indicating a definite need for more objective methods of rating clinical signs.[8-13] There is general agreement that a single stigma is rarely diagnostic of a specific vitamin deficiency and that combinations or patterns of associated stigmata are preferable.[14] It is hoped (1) that this paper will evoke further interest in more descriptive criteria and (2) that the method of tabulation presented will promote and facilitate the study of relative frequencies of gross tissue abnormalities associated with vitamin deficiencies.

This study is one of a series investigating relationships between physical signs of vitamin deficiency, blood serum levels, and nutrient intakes as used to assist in the diagnosis, treatment, and prevention of vitamin deficiencies.[15-18] Presented first is a detailed description of the criteria used in classifying children into three study groups; namely (1) a Control Group exhibiting no or minimum signs suggestive of vitamin deficiency, (2) a Vitamin A Deficiency Group exhibiting widely accepted signs suggestive of vitamin A deficiency, and (3) an Ascorbic Acid Deficiency Group exhibiting widely accepted signs suggestive of ascorbic acid deficiency. Secondly, the frequency of stigmata with their degree of severity are shown. Lastly, a method of analyzing combinations of stigmata with regard to their degree of severity, and distribution within the combinations is demonstrated. Relationships between blood serum levels and nutrient intakes of these three groups are reported in another paper.[19]

PROCEDURE

In the fall of 1949, children under 12 years of age in the 4th, 5th, and 6th grades in Bur-

This research work was a co-operative project between the Departments of Biochemistry and Anatomy, College of Medicine, and the Agricultural Experiment Station, University of Vermont and State Agricultural College. Vermont Agricultural Experiment Station Journal Series Paper No. 39.

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lington, Vermont, were screened by a physician having considerable training and experience in nutritional aspects of clinical medicine. After the children selected were examined to determine stigma severity and those taking vitamin supplements excluded, 25 qualified for the Control Group, 22 for the Vitamin A Group, and 32 for the Ascorbic Acid Group. Heights and weights of children in the above groups were recorded at the time of examination. In the spring of 1950, a similar examination was made, and only those subjects were retained who met the criteria used for the initial classification. Thus, 25 finally qualified for the Control Group, 21 for the Vitamin A Group, and 25 for the Ascorbic Acid Group.

The degrees of severity of physical stigmata were designated as "very mild" (±), "mild" (+), "moderately severe" (++), and "markedly severe" (+++). Rating of stigmata according to degree was based on the severity of the condition rather than on the amount of tissue area involved or the stage of the process, that is, acute or chronic. The term "slight" indicated a condition apparent after close examination, while the term "obvious" indicated a condition apparent at first glance. An 8-inch focal length head loupe "Magni-Focuser" was used in these examinations. Subsequent experience in recording and studying tissue changes has shown that colored photographs and use of duplicate projectors for purposes of comparisons are more satisfactory than written records. The criteria of stigmata used in classifying the subjects into the three groups were as follows:[14,20-23]

STIGMATA OF VITAMIN A DEFICIENCY

SKIN: (Postero-lateral aspects upper limbs and antero-lateral aspects lower limbs)

Follicular Hyperkeratosis:

±	Slight—very few scattered hyperkeratotic follicles barely palpable when in contact with warm hand.
+	Slight—few such follicles palpable when in contact with warm hand.
++	Obvious—rough, graterlike surface easily palpable.
+++	Obvious—intensity greater than ++ with protruding horny papules formed by keratotic plugs.

Xerosis:

Dryness

±	Slight—no detection of normal oily sheen of skin.
+	Slight—grayish powdery appearance lacking normal sheen.
++	Obvious—definite powdery appearance.
+++	Obvious—intensity greater than ++ giving a loose, powdery, granular appearance.

Scaling

±	Slight—skin beginning to scale.
+	Obvious—as above.
++	Obvious—scales with flakes shedding.
+++	Obvious—intensity greater than ++ with free shedding.

Crinkling

±	Slight—faint alligator scalelike pattern.
+	Obvious—same as above.
++	Obvious—well-defined pattern.
+++	Obvious—well-defined pattern with easily observed grooved boundary markings.

EYES: (Bulbar conjunctiva's superficial and deep layers in nasal and temporal zones were examined by moving the lower lid over the conjunctiva watching for layers of blood vessels to determine the presence of thickening that masks normal bluish tinge.)

Transparency:

tr	Normal blue tint of sclera easily seen on examination.

Translucency:

tl_0	Slight—clouding obviously masking blue tint with blood vessels readily visible, but limited to corners of zones.
tl_1	Slight—same as above, but throughout entire zones.
tl_2	Obvious—clouding obviously masking blue tint of sclera and blood vessels barely seen.

STIGMATA OF ASCORBIC ACID DEFICIENCY

GUMS: (Upper and lower gums were examined)

Blunting:

±	Papilla reduced in height to one-fourth normally exposed surface of adjacent teeth.
+	Papilla reduced from one-fourth to just above normal baseline of marginal gingiva.
++	Papilla at or beyond level of normal marginal gingiva. (Blunting was disregarded if spacing of teeth was 1 mm. or more at sites of their marginal gingivae.)

Swelling: (Temporary pitting following momentary firm pressure with bare flat end of applicator stick confirms swelling.)

±	Slight—puffiness barely evident.
+	Obvious—puffiness evident.
++	Obvious—swelling giving a very smooth, plump, puffy, spongy appearance.

Thickening: (A sensation of hardness obtained by momentary firm pressure with bare flat end of applicator stick confirms thickening.)

± Slight—enlarged firm appearance of papilla and/or marginal gingiva.

\+ Obvious—appearance of firm collar on papilla and/or marginal gingiva enlarged beyond normal.

++ Obvious—straight wide bandlike appearance of gum being firm, hard, and tight in its gross enlargement.

Recession:

± Slight—marginal gingiva barely atrophied beyond the normal level.

\+ Obvious—atrophied into marginal gingiva.

++ Obvious—atrophied beyond marginal gingiva.

+++ Obvious—atrophied well into and possibly throughout alveolar gingiva.

Punctate Depressions:

± Slight—minute pin-point depressions barely seen on gum surface.

\+ Obvious—pin-point depressions easily seen.

++ Obvious—gross pin-point depressions easily seen.

Retraction:

\+ Obvious—gum extended away from tooth.

++ Obvious—extent greater than +.

Bleeding:

Pressure—immediate bleeding at site after momentary firm pressure of applicator stick.

Spontaneous—bleeding present upon display of gums.

Additional criteria used in selecting cases for the Control Group were as follows:

Skin area:

Face—acne, sebaceous plugs, and greasiness.

Naso-labial folds, and behind and above ears—redness and seborrhea.

Hair, scalp and nails—abnormalities.

Eyes:

Pigmentation, circumcorneal and conjunctival injection, hypertrophied follicles, blepharitis, photophobia, and lacrimation

Tongue:

In general—abnormal color, edema, indentations, serrations, and fissures.

Fungiform and filiform papillae—hypertrophy, flattening, fusion or atrophy.

Lips:

Vertical markings, scaling, thinning, swelling, fissures, maceration, scarring, and abnormal color.

Gums:

Tenderness, consistency, and redness.

Children selected for inclusion in the Vitamin A and Ascorbic Acid Groups were required to exhibit signs associated with the respective deficiency. At least one sign had to be of a moderate or marked degree of severity. No children were included in the Control Group who exhibited more than a mild degree of severity of all criteria with the exception of eight, one having moderate lacrimation, moderate thinning and vertical markings of lips; one, moderate thinning of lips; four, moderate vertical marking of lips; and two, moderate blunting of interdental papillae.

Results

The total frequency and severity of individual stigmata of the Control and Ascorbic Acid Groups, and the Control and Vitamin A Groups are shown in Tables I and IV. Tables II and III present the combinations of ascorbic acid deficiency signs with their severity for the Control and Ascorbic Acid Groups, while in Tables V and VI the combinations of vitamin A deficiency signs with their severity for the Control and Vitamin A Groups, respectively, are seen. These results are expressed as percentages based on the total number of subjects (Tables I and IV) in each group in the fall and spring. Such tabulations make it possible to determine how the Control Group differs from the Deficiency Groups, and whether all three groups have the same stigma patterns in the fall and spring. A few of the more obvious findings demonstrating this method of analyzing physical stigmata suggestive of vitamin deficiency are reported.

Table I shows that the Control Group in general had a larger proportion of cases with blunting and pitting than of the other stigmata studied, while the Ascorbic Acid Group had more cases with blunting, pitting, thickening, swelling, and recession than retraction and bleeding. The seasonal pattern shows the Control Group had more blunting and thickening in the fall than spring, but pitting, swelling and recession show the reverse. The Ascorbic Acid Group also had more blunting and thickening as well as recession and bleeding in the fall than spring, but again incidence of

TABLE I

Control and Ascorbic Acid Groups
(Frequency of Ascorbic Acid Deficiency Stigmata)

	Control Group				Ascorbic Acid Group			
	Fall		Spring		Fall		Spring	
	No. 25	% 100	No. 25	% 100	No. 32	% 100	No. 25	% 100
Physical Signs								
No signs	1	4	2	8	..	..	..	..
Blunting								
± & +	22	88	16	64	11	34	13	52
++ & +++	1	4	1	4	17	53	5	20
Pitting								
± & +	20	80	22	88	26	81	24	96
++ & +++	..	..	..	..	2	6	..	..
Thickening								
± & +	10	40	3	12	5	16	3	12
++ & +++	..	..	..	..	25	78	10	40
Swelling								
± & +	1	4	4	16	12	38	9	36
++ & +++	..	..	..	..	14	44	13	52
Recession								
± & +	1	4	2	8	9	28	7	28
++ & +++	..	..	..	..	20	63	14	56
Retraction								
± & +	..	..	..	..	2	6	2	8
++ & +++	..	..	..	..	..	..	1	4
Bleeding								
Pressure	..	..	..	..	6	19	3	12
Spontaneous	..	..	..	..	3	9	2	8

pitting and swelling along with retraction was reversed. The Control Group had no or a mild degree of severity with the exception of one subject, and a lesser number of ascorbic acid deficiency signs, whereas the Ascorbic Acid Group had a greater proportion of cases with moderate to marked degrees of severity, and more of the various stigmata. Retraction and bleeding appear only in the latter group.

From data in Table II, we find the Control Group had the larger proportion of subjects in the Two and Three Combinations of stigmata. Within these combinations and, in general, blunting and pitting are seen most frequently, while the other signs are distributed as shown. Little difference in seasonal pattern appeared; however, the Four Combination was added in the spring.

Study of Table III reveals that the Ascorbic Acid Group had the larger proportion of subjects in the Four, Five, and Six Combinations of stigmata. Within these combinations, where retraction and bleeding occurred, the majority of subjects had moderate to marked degrees of stigma severity. A greater proportion of cases showed more thickening in the fall than spring, but except for blunting there were tendencies for the remaining signs to be reversed. Throughout all combinations, a greater proportion of cases showed recession and pitting.

From Table IV, it is seen that in the Control Group translucency in the corners of the bulbar conjunctivae occurred more frequently than any of the other four stigmata studied. In the Vitamin A Group, all subjects had follicular hyperkeratosis and dryness. The Control Group showed a lower incidence of the five stigmata in the fall than spring except for follicular hyperkeratosis which remained the same. For the Vitamin A Group, translucency throughout the bulbar conjunctivae and crinkling occurred more frequently in the fall than spring, but scaling showed the reverse. The Control Group in general had fewer cases showing these stigmata, all of a

TABLE II

Control Group

Combinations of Ascorbic Acid Deficiency Stigmata

	None				One				Two				Three				Four			
	F		S		F		S		F		S		F		S		F		S	
	No. 1	%* 4	No. 2	% 8	No. 2	% 8	No. 6	% 24	No. 13	% 52	No. 11	% 44	No. 9	% 36	No. 4	% 16	No. 0	% 0	No. 2	% 8
Physical Signs																				
Blunting																				
± & +					1	4	1	4	7	28	10	40	9	36	4	16	..	..	1	4
++ & +++					..	..	..	..	1	4	..	..	..	..	..	..	..	..	1	4
Pitting																				
± & +					1	4	5	20	11	44	11	44	8	32	4	16	..	..	2	8
++ & +++																				
Thickening																				
± & +									2	8	1	4	8	32	2	8	..	..	..	..
++ & +++																				
Swelling																				
± & +													1	4	2	8	..	..	2	8
++ & +++																				
Recession																				
± & +													1	4	..	..	..	..	2	8
++ & +++																				
Retraction																				
± & +																				
++ & +++																				
Bleeding																				
Pressure																				
Spontaneous																				

* Percentages are based on the total number—Fall 25, Spring 25.

TABLE III

Ascorbic Acid Group
Combinations of Ascorbic Acid Deficiency Stigmata

	Two				Three				Four				Five				Six			
	F		S		F		S		F		S		F		S		F		S	
	No.	%*	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%
	0	0	1	4	3	9	2	8	10	31	10	40	13	41	10	40	6	19	2	8
Physical Signs																				
Blunting																				
± & +			..	..	1	3	2	8	3	9	5	20	3	9	7	28	4	13	1	4
++ & +++			..	..	..	..	..	..	5	16	1	4	10	31	2	8	2	6	1	4
Pitting																				
± & +			1	4	3	9	..	..	7	22	9	36	10	31	10	40	6	19	2	8
++ & +++			..	..	..	..	..	..	..	..	..	..	2	6	..	..	..	..	..	..
Thickening																				
± & +			..	..	..	..	..	..	1	3	..	..	1	3	3	12	3	9	..	..
++ & +++			1	4	3	9	2	8	9	28	4	16	10	31	3	12	3	9	..	..
Swelling																				
± & +					..	..	..	..	2	6	3	12	7	22	4	16	3	9	2	8
++ & +++					1	3	1	4	3	9	6	24	5	16	6	24	3	9	..	..
Recession																				
± & +					1	3	1	4	2	6	3	12	4	13	3	12	2	6	..	..
++ & +++					..	..	..	..	7	22	7	28	9	28	7	28	4	13	2	8
Retraction																				
± & +									1	3	..	..	1	3	..	..	1	3	1	1
++ & +++									..	..	..	..	..	..	..	..	..	..	4	4
Bleeding																				
Pressure									..	..	..	..	1	3	3	12	5	16	2	8
Spontaneous									1	3	..	..	2	6	2	8	..	..	..	..

* Percentages are based on the total number—Fall 32, Spring 25.

TABLE IV

Control and Vitamin A Groups
Frequency of Vitamin A Deficiency Stigmata

	Control Group				Vitamin A Group			
	Fall		Spring		Fall		Spring	
	No. 25	% 100	No. 25	% 100	No. 22	% 100	No. 21	% 100
Physical Signs								
No signs	8	32	4	16	..	..	..	..
Conjunctivae:								
Bulbar								
tl_o	11	44	16	64	2	9	..	..
tl	..	..	..	..	17	77	13	62
Follicular Hyperkeratosis								
± & +	5	20	5	20	..	..	..	..
++ & +++	..	..	..	..	22	100	21	100
Xerosis:								
Dryness								
± & +	6	24	10	40	14	64	13	62
++ & +++	..	..	..	..	8	36	8	38
Crinkling								
± & +	..	..	1	4	9	41	8	38
++ & +++	..	..	..	.	6	27	3	14
Scaling								
± & +	2	8	3	12	16	73	17	81
++ & +++	..	..	..	..	2	9	3	14

mild degree of severity, than the Vitamin A Group, where a majority had a moderate to marked degree of severity for follicular hyperkeratosis.

It is apparent from study of Table V that the Control Group had the larger proportion of subjects in the None and One Combinations with translucency in the corners of the bulbar conjunctiva appearing most frequently. Differences in seasonal pattern may be seen in this tabulation.

Lastly, Table VI shows that the Vitamin A Group had the larger proportion of cases in the Four and Five Combinations with all cases in the Five Combinations exhibiting the entire number of signs studied. All combinations exhibited follicular hyperkeratosis and dryness. Again, differences in seasonal pattern within the different combinations are apparent.

Heights and weights were analyzed, since they are frequently used in judging the nutritional status of children. There were three height-weight classifications, namely (1) "normal weight"—within normal height and weight range, (2) "underweight"—within normal height range but below normal weight range, and (3) "overweight"—within normal height range but over normal weight range.[24] If the subject was above or below the normal height for his age, age was disregarded and normality of weight judged on the basis of the weight range where his height first appeared in the table. The Control Group contained 4 per cent underweight, 52 per cent normal weight, and 44 per cent overweight children; the Vitamin A and Ascorbic Acid Groups were very similar and combined had 4, 54, and 42 per cent, respectively, which indicated no marked difference in the percentage distribution between these Groups.

An examination of data for heights according to age revealed that in the Control Group there were 56 per cent in the normal height range, 12 per cent below and 32 per cent above. Corresponding percentages for the Vitamin A Group were 50, 9 and 41 per cent and for the Ascorbic Acid Group were 56, 28 and 16 per cent. It is interesting to note that the Ascorbic Acid Group had a larger proportion of children in the underheight and a smaller proportion in the overheight class than did the Control or Vitamin A Group. The majority

TABLE V

Control Group

Combinations of Vitamin A Deficiency Stigmata

	None				One				Two				Three				Four			
	F		S		F		S		F		S		F		S		F		S	
	No. 8	%* 32	No. 4	% 16	No. 14	% 56	No 11	% 44	No. 1	% 4	No. 6	% 24	No. 0	% 0	No. 4	% 16	No. 2	% 8	No. 0	% 0
Physical Signs																				
Conjunctivae:																				
Bulbar																				
tl_e					8	32	9	36	1	4	4	16	..	..	3	12	2	8		
tl					..	..	..	..	..	..	..	..	..	..	..	..	..	..		
Follicular Hyperkeratosis																				
± & +					3	12	..	..	..	..	3	12	..	..	2	8	2	8		
++ & +++					..	..	..	..	..	..	..	..	..	..	..	..	..	..		
Xerosis:																				
Dryness																				
± & +					3	12	2	8	1	4	4	16	..	..	4	16	2	8		
++ & +++											..	..	..	..	..	..	..	..		
Crinkling																				
± & +											..	..	..	..	1	4	..	..		
++ & +++											..	..	..	..	..	..	..	..		
Scaling																				
± & +											1	4	..	..	2	8	2	8		
++ & +++											..	..	..	..	..	..	..	..		

* Percentages are based on total number—Fall 25, Spring 25

TABLE VI

Vitamin A Group

Combinations of Vitamin A Deficiency Stigmata

	Two				Three				Four				Five			
	F		S		F		S		F		S		F		S	
	No. 1	%* 5	No. 0	% 0	No. 2	% 9	No. 4	% 19	No. 7	% 32	No. 10	% 48	No. 12	% 55	No. 7	% 33
Physical Signs																
Conjunctivae:																
bulbar																
tl_e	..	..	..	..	..	..	..	..	1	5	..	..	1	5	..	..
tl	..	..	..	..	1	5	..	..	5	23	6	29	11	50	7	33
Follicular Hyperkeratosis																
± & +	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..
++ & +++	1	5	..	..	2	9	4	19	7	32	10	48	12	55	7	33
Xerosis:																
Dryness																
± & +	1	5	..	..	2	9	2	10	5	23	7	33	6	27	4	19
++ & +++					..	..	2	10	2	9	3	14	6	27	3	14
Crinkling																
± & +					1	5	..	..	2	9	3	14	6	27	5	24
++ & +++							..	..	..	..	1	5	6	27	2	10
Scaling																
± & +							2	10	6	27	9	43	10	45	6	29
++ & +++							2	10	..	..	1	5	2	9	1	5

* Percentages are based on total number—Fall 22, Spring 21.

of these underheight children had weights normal for their heights and so fell into the normal height-weight range.

Summary

To stimulate further interest in methods of appraising clinical signs of vitamin deficiencies, a detailed description and analysis of the criteria used in classifying children exhibiting (1) no or very mild signs suggestive of vitamin deficiency, (2) widely accepted signs suggestive of vitamin A deficiency, and (3) widely accepted signs suggestive of ascorbic acid deficiency is presented.

Conclusions

On using incidence of stigmata only, a majority of the control children could have been included in a deficiency group, since they had one or more of the associated signs of vitamin A or ascorbic acid deficiency. By noting degree of severity along with incidence, group differences became apparent. By use of combinations of signs along with incidence and severity, characterization of and differentiation between the three groups were defined.

Examinations of the frequency and combinations of stigmata according to their degree of severity showed that the Control Group and Deficiency Groups were sufficiently different to make feasible a comparison of serum levels and nutrient intakes between these groups.

This method of recording incidence of combinations of physical signs revealed information masked by tabulations showing total frequency only.

Combinations of individual signs in each of the three groups were for the most part similar in the fall and spring, although there is variation in the percentage distribution.

The small proportion of underweight cases with nearly equal distribution in the normal and overweight classes and the fact that the three groups were similar in height-weight distribution suggests that one should be cautious about correlating such data with physical signs of vitamin A and ascorbic acid deficiency.

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RESUMEN

Sobre los estigmas físicos atribuídos a las deficiencias de vitamina A y ácido ascórbico

Con el objeto de estimular interés en los métodos clínicos de apreciación de deficiencias vitamínicas se presenta una descripción detallada y un análisis de los criterios usados en la clasificación de niños que presentaban: (1) ningun o muy ligeros signos sugestivos de deficiencia vitamínica, (2) signos ampliamente aceptados como sugestivos de deficiencia de vitamina A, y (3) signos comunmente aceptados como sugestivos de deficiencia de ácido ascórbico.

Utilizando solamente la incidencia de estigmas, la mayoría de los niños control podían ser incluídos en el grupo con deficiencia, ya que presentaban uno o más de los signos asociados de la deficiencia de vitamina A o ácido ascórbico. Si se consideraban el grado de severidad de los signos juntamente con la incidencia, entonces la diferenciación de los grupos se volvía aparente. Utilizando la combinación de los signos juntamente con la severidad y la incidencia, la caracterización y la diferenciación entre los tres grupos era claramente definida.

Exámenes de la frecuencia y combinación de los estigmas de acuerdo con el grado de severidad mostraron que los grupos deficientes y control fueron suficientemente diferentes

para hacer factible una comparación de los niveles serológicos y la ingestión nutritiva entre estos grupos.

Este método de anotación de la incidencia de combinaciones de signos físicos reveló una información enmascarada por cálculos que demostraban solamente la frecuencia total.

Combinaciones de los signos individuales en cada uno de los tres grupos fueron en su mayor parte similares, aunque existe una variación en los porcentajes de distribución de aquellos.

La pequeña proporción de casos con falta de peso, con una distribución aproximadamente igual en los clases con peso normal o sobrepeso, y dado el hecho de que los tres grupos fueron similares en lo referente a la distribución de peso y altura sugiere que se debe tener mucha cautela al correlacionar estos datos con los signos físicos de deficiencia de vitamina A y ácido ascórbico.

What is Health?

"There have been many attempts to define what we mean by health, but none of them seems quite satisfactory. I do not think it matters very much. It is likely that my ideas are pickled with prejudice, but I think that health is very much a personal matter, always elusive, and as manifold as there are people on this earth. Everyone wants, and should have, health according to his own individual personality and need—that is, within the usual limits of freedom; but he will not attain this by too great an interest in his health, and his interest does become too great when it is stimulated by mass enthusiasm."
—W. J. Saxton in an Address to the Queensland Branch of the British Medical Association. *The Medical Journal of Australia* II (15): 558, 1953.

The Simple—and the Secret

"All the great problems that have perplexed the medical profession in the past have had simple explanations, but possibly less than one per thousand of those engaged on the problems had even an inkling of their solution."
—A. K. Maxwell. *The Medical Press* 230 (6): 154, 1953.

In Defense of Research

"If an ounce of practice is worth a ton of theory, then an ounce of research is equally worth a ton of unthinking practice. Anyone who feels inclined to dispute this equation should reflect on the countless numbers of persons formerly engaged, for example, in the treatment of diphtheria as compared to the relatively few people employed by the research authorities in preparing and refining the diphtheria toxin, in evaluating its effects, and in finally contriving an efficient antigen. The ratio between the time occupied in research all over the world on this problem since its inception, and the time that would have been spent in this country alone within the past ten years had these researches not been carried out, reveals what enormous dividends we have reaped from these brilliantly successful inquiries. Leaving time values for the moment, and concentrating on money values, the expenditure on research in this field alone must have paid for itself a thousand-fold even by now. In short, whether we reckon in terms of time or money, or in the humanitarian currency of lives saved and suffering averted, there cannot be a moment's hesitation in reaching the conclusion that nothing pays such bountiful and profitable dividends as research."
—Editorial. *The Medical Press* 230 (9): 201, 1953.

Relationships Between PHYSICAL SIGNS *OF* DEFICIENCY, BLOOD LEVELS, *and* FOOD INTAKES *with Respect to* VITAMIN A *and* ASCORBIC ACID *in Selected Groups of Children*

By

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IN A PREVIOUS investigation, a study was made of relationships between certain serum vitamin levels and nutrient intakes of children with physical signs of various vitamin deficiencies.[1-4] The question arose as to whether there were differences in serum levels and nutrient intakes between children with no or minimum physical stigmata and those with physical stigmata suggestive of vitamin A and ascorbic acid deficiencies.[5]

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PROCEDURE

The procedure used in this study was the same as that described in the companion paper.[6]

Non-fasting blood samples were taken between 9:00 and 10:00 a.m. in the fall and spring. Serum levels of carotene, vitamin A, and ascorbic acid were determined by microchemical techniques.[7,8]

A record of all food eaten during the preceding 24 hours was secured by the recall method in individual interviews on the same day the blood samples were collected. The interview was conducted under such circumstances as to minimize motives that might tempt the subject to distort the report of what he ate. The child was seen alone in familiar surroundings. Rapport was established between the interviewer and subject. Ample opportunity was allowed for questions and discussion. A quantitative estimate of food consumed was facilitated by use of food models, dishes, and utensils similar to those used by the subject at home. Suggestion was avoided by using the models only after the record of food eaten was secured. The nutrient intake was calculated for each individual.[9] All cases used in the fall and spring

had complete data for physical findings, blood analyses, and nutrient calculations.

Results and Discussion

The mean serum levels of vitamin A and carotene for the Control and Vitamin A Groups, and of ascorbic acid for the Control and Ascorbic Acid Groups in the two seasons, are presented in Table I. The differences in mean serum levels of the Control versus the Deficiency Groups were not significant except for carotene in the Control and Vitamin A Groups. However, the mean levels of the Control Group were higher than those of the Deficiency Groups, with the exception of the ascorbic acid level in the fall. In five of the six comparisons made, the Control Group had higher means, two significant. In only one case was the mean level of a deficiency group higher and this insignificantly so.

The percentage of serum levels above or below the lower value of the "good" range in Bessey's classification were computed[10] (Table II). These percentages were then used to compare differences between groups and seasons. The Control Group had a significantly higher percentage of cases in the upper range for vitamin A, and ascorbic acid in the spring than did the Deficiency Groups. This was true for carotene values in the fall, but in the spring only a tendency in this direction was found. In other words, in four of the six comparisons made, the Control Group had a higher proportion of cases in the upper range, three of which were statistically significant, while in the remaining two comparisons, the deficiency groups had an insignificantly higher proportion of cases in the upper range.

TABLE I

Mean Serum Levels According to Group and Season

	Fall 1949	Spring 1950	
	Vitamin A Levels (μg. per 100 cc.)		Seasonal "t"
Control Group	38 ± 16	45 ± 14	1.631
Vitamin A Group	37 ± 15	42 ± 16	0.967
Group "t"	0.217	0.718	...
	Carotene Levels (μg. per 100 cc.)		
Control Group	161 ± 41	186 ± 53	1.824*
Vitamin A Group	127 ± 48	137 ± 36	0.701
Group "t"	2.547†	3.528‡	...
	Ascorbic Acid Levels (mg. per 100 cc.)		
Control Group	0.83 ± 0.43	1.17 ± 0.49	2.556†
Ascorbic Acid Group	0.85 ± 0.53	0.94 ± 0.55	0.603
Group "t"	0.137	1.536	

* P 10%. † P 2%. ‡ P 1%. This means that the probability that this association could be due to chance is 10 out of 100, 2 out of 100, etc.

Instances where no differentiation could be found between Control and Deficiency Groups by serum level comparisons may be due to (1) a lack of specificity in the physical signs of vitamin A and ascorbic acid deficiencies, (2) the possibility that serum levels obtained at the time of the physical examination do not reflect the deficiency which originated in the past, (3) too little difference between vitamin A and ascorbic acid nutriture, or (4) the possibility that the dividing lines for serum levels were set too high. An explanation may be that Bessey's classification is not based on clinical findings and the ranges may not be suitable for evaluating nutritional status with respect to a given nutrient.

Lack of correlation between certain biochemical and clinical findings has also been reported by Kark *et al.*,[11] Krause and Pierce,[1] Riggs *et al.*,[12] Youmans *et al.*,[13,14] and Anderson and Milam.[15]

Goldsmith[16] states that in the majority of studies, little or no correlation has been demonstrated between the amounts of ascorbic acid in the plasma or the degree of saturation of the tissues with vitamin C, and changes in the gums ascribed to deficiency of this nutrient. Dann and Darby[17] point out that the interpretation of nearly all biochemical tests used in the appraisal of nutritional status in humans is uncertain because these tests have not been correlated with the production and cure of the clinical signs of the disease in human subjects. Current investigations in this laboratory are designed to provide additional

TABLE II

Independence Test of Serum Levels for Group and Season

	Fall 1949				Spring 1950				Season Chi-sq.
	No.	%	No.	%	No.	%	No.	%	
Vitamin A Levels (μg. per 100 cc.)									
	<30		≥30		<30		≥30		
Control Group	8	32	17	68	3	12	22	88	3.722
Vitamin A Group	6	27	16	73	6	29	15	71	...
Group Chi-sq.	0.053				4.086*				
Carotene Levels (μg. per 100 cc.)									
	<125		≥125		<125		≥125		
Control Group	4	16	21	84	5	20	20	80	0.075
Vitamin A Group	14	64	8	36	6	29	15	71	8.531†
Group Chi-sq.	33.972†				0.503				
Ascorbic Acid Levels (mg. per 100 cc.)									
	<0.7		≥0.7		<0.7		≥0.7		
Control Group	12	48	13	52	5	20	20	80	6.771†
Ascorbic Acid Group	13	41	19	59	12	48	13	52	0.375
Group Chi-sq.	0.451				10.563†				

*P 5%. †P 1%.

information about this type of correlation.

Inconsistencies of comparisons made in the fall and spring led to an investigation of seasonal differences in serum levels of the individual groups. Table I shows the seasonal comparisons for the Control, Vitamin A, and Ascorbic Acid Groups, and leads one to suspect that a seasonal influence may affect the results of group comparisons. The mean serum levels tended to be higher in the spring, although significantly so only in the Control Group for carotene and ascorbic acid. While seasonal differences in serum levels have been demonstrated by other workers,[18] the findings are controversial.[19,20]

In the spring, the Vitamin A Group had a significantly greater proportion of cases in the upper range for carotene. Also in the spring, the Control Group had a significantly greater proportion of cases in the upper range for ascorbic acid and vitamin A, although the vitamin A was at a lesser degree of significance (Table II).

It was only with the ascorbic acid serum levels of the Control Group that both the means and proportions were significantly higher in the spring. Inconsistencies indicate that the interpretation of data may depend on the method of statistical analysis used.

The results of seasonal comparisons suggest that serum levels were not the same in the spring as in the fall, particularly for the Control Group. Combining the results of the two seasons might very well have invalidated the findings.

Table III shows no significant difference in the mean nutrient intakes of the groups, although the values for the Control Group tended to be higher. However, the wide variability of the individual intakes as indicated by the large standard deviations make it difficult to interpret the findings.

Approximately two-thirds of the cases did not meet the National Research Council recommended daily dietary allowances of vitamin A and ascorbic acid.[21]

Since a single 24-hour food record is not considered a reliable indication of the individual's overall food intake,[22] chi-square tests were not carried out on the nutrient intake data as they were on serum level data.

Seasonal differences in mean nutrient intake were not significant (Table III); however, such differences have been noted by other workers.[23,24]

The association between serum levels and nutrient intakes for each group is reported in Table IV. Significant results are limited to

TABLE III

Mean Nutrient Intakes According to Group and Season*

	Fall 1949	Spring 1950	
	Vitamin A Valuse (I.U.)		Seasonal "t"
Control Group	162 ± 128	122 ± 112	1.163
Vitamin A Group	140 ± 131	120 ± 106	0.551
Group "t"	0.571	0.060	
	Ascorbic Acid Values (mg.)		
Control Group	1.90 ± 1.16	2.10 ± 1.53	0.949
Ascorbic Acid Group	1.86 ± 1.13	1.40 ± 1.10	1.508
Group "t"	0.129	1.823†	

* Nutrient intakes per kilogram body weight.
† P 10%.

ranged from 0.13 to 2.63 mg. per 100 cc. and the intakes from 0.3 to 8.0 mg. per kilo. Merrow *et al.*,[2] studying children (8 to 15 years old), did not find relationships between serum levels of vitamin A and nutrient intake of vitamin A *per se*.

In a study of 95 children, Szymanski and Longwell[19] found no significant correlation between plasma levels and dietary sources of vitamin A alone, whereas they found plasma carotene had a highly significant correlation with vitamin A (carotene) intake from plant sources. Williams *et al.*[20] observed "in general the higher the vitamin A value of the diet the higher the average level of both serum carotene and vitamin A." Urbach *et al.*[26] suggest that plasma vitamin levels are affected more by nonvitamin factors in the diet, environment, or *in vivo* than by the vitamins themselves.

TABLE IV

Correlation Coefficient Association Between Nutrient Intakes and Serum Levels

	Nutrient intakes*	Serum levels†	Fall 1949, "r" values	Spring 1950, "r" values
Control Group	Vitamin A	Vitamin A	0.079	0.023
	Vitamin A	Carotene	0.247	0.299
	Ascorbic Acid	Ascorbic Acid	0.136	0.474‡
Vitamin A Group	Vitamin A	Vitamin A	0.165	0.095
	Vitamin A	Carotene	0.207	0.069
Ascorbic Acid Group	Ascorbic Acid	Ascorbic Acid	0.453**	0.055

* Nutrient intakes (per kilogram body weight) expressed: Vitamin A, I.U.; Ascorbic Acid, mg.
† Serum levels expressed: Vitamin A and Carotene, μg. per 100 cc.; Ascorbic Acid, mg. per 100 cc.
‡ P 5%.
** P 1%.

The nutriture of an individual is the result of the adequacy or inadequacy of his nutrient intake and utilization over various periods of time. Only if current serum levels and nutrient intakes reflect the past history can they be related to the present state of nutrition. This problem of relationships between serum levels, nutrient intakes, and physical signs of vitamin deficiencies is well recognized. No doubt the dissimilarity of techniques and methods used in various studies confuses the interpretation of findings. Improved techniques of collecting, analyzing, and interpreting such data are being developed.[24,27,28] Of particular interest is a

ascorbic acid; that is, there was a positive relationship between the ascorbic acid intake and the ascorbic acid blood level in the subjects with vitamin C deficiency signs in the fall and a similar relationship in the Control Group in the spring. All correlations, however, were found to be positive. The intake of ascorbic acid is reflected in serum or plasma ascorbic acid as shown by other workers. Bryan *et al.*[25] showed that in healthy human subjects (12 to 35 years old) "saturation with a plasma concentration of approximately 1.0 mg. per 100 cc. occurs with intakes of 1.7 to 1.9 mg. ascorbic acid per kilo. With lower intakes the plasma level (fasting) varies directly with the intake; higher intakes cause little further increase in the plasma." Data in this paper do not reveal such an abrupt change between intake and the serum level of ascorbic acid, although the serum levels

method of determining the number of food intake records required for a more valid estimate of nutrient intake.[29]

Unfortunately, the number of subjects studied was smaller than originally planned, due to elimination of cases taking vitamin supplements. The spring period was in May and June, but the fall period extended into December, which in this area may be considered winter, and thus may have masked possible seasonal differences between fall and spring. Larger number of subjects, repeated food intake records and serum determinations, and earlier collections of fall values might have shown more meaningful or definite relationships.

Conclusions

Under the conditions and by the methods described, differentiation could be made only by mean carotene levels between a group of children exhibiting moderate to severe degrees of physical signs suggestive of vitamin A deficiency and a control group of children showing no or mild degrees of the same physical signs. The mean vitamin A levels, however, suggested such a differentiation. Comparisons of mean ascorbic acid levels were inconclusive when similarly used for the Ascorbic Acid and Control Groups.

Although the intakes of vitamin A and ascorbic acid tended to be higher for the Control than for the Deficiency Groups, nutrient intake did not afford a satisfactory method of differentiation.

Associations between nutrient intakes and serum levels are not uniformly significant, yet all are positive and suggest relationships.

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Resumen

Relación entre los signos físicos de deficiencia, los niveles hemáticos y la ingestión de alimentos con respecto a la vitamina A y el ácido ascórbico en un grupo seleccionado de niños

Bajo las condiciones y métodos descritos la diferenciación pudo hacerse solamente con respecto a los niveles de carotene entre un grupo de niños que presentaban desde grados moderados hasta severos signos físicos que sugerían una deficiencia de vitamina A y un grupo control de niños que no demostraban, o solamente tenían ligeros grados de los mismos signos físicos. Los niveles hemáticos, sin embargo, sugerían tal diferenciación. Los resultados obtenidos no fueron satisfactorios cuando se hicieron estudios similares con respecto al uso de ácido ascórbico y los grupos control.

Aunque la ingestión de vitamina A y ácido ascórbico tendía a ser mayor en el grupo control que en el grupo que presentaba signos de deficiencia, la ingestión de una dieta nutritiva no demostró ser un método satisfactorio de diferenciación.

La asociación entre una ingestión nutriva y los niveles serológicos no son uniformemente significantes, aunque todos son positivos y sugieren algunas relaciones.

Patient's Dilemma

"Doctors who have been fortunate enough to escape illness do not realize that it is not always easy to describe accurately the location and nature of subjective sensory disturbances. With the doctor, whose greatest enemy is time, the patient runs the danger of falling between two stools: of appearing disturbingly vague in his recital of dates of onset, site, severity, development of symptoms; or of appearing obsessional and hypochondriacal if he has kept a diary of the evolution of his illness."

—I. Atkin. *The Medical Press* 230 (10): 235, 1953.

A LOW-COST, HIGH PROTEIN, LOW CALORIE FOOD

By BARNETT SURE, PH.D.*

PROTEIN deficiency occurs among large populations in many parts of the world and among appreciable portions of the populations even in well-nourished countries like the United States. The low life expectancy in the Far East, in Central America, and in large areas of South America may very well be correlated with protein deficiency. A deficit of food proteins also afflicts large sections of Africa and Europe.

The great deficiency of proteins in Europe caused by the last World War and the increasing costs of meats in this country stimulated the author to develop a low-cost high protein food.† The earlier products contained a rather complicated formula, the base of which was dry nonfat milk solids supplemented with significant amounts of defatted soya flour and appreciable portions of food yeast, whole wheat, and vegetable shortening. They were also supplemented with iron and calcium salts and vitaminized with thiamine, riboflavin, and niacin. The increasing costs of the dry milk necessitated a change in the formula, which was later simplified. The preparation now has as its base defatted soya flour and contains significant amounts of dry nonfat milk solids, some roughly ground whole wheat, and vegetable shortening. It is spiced with tomato catsup, and vitaminized with thiamine, riboflavin, and niacin. After the dry ingredients are mixed with a certain amount of water and processed for one hour at 15 lb. pressure, the food becomes a solid with a golden-brown color. It has a definite meaty texture, a nutty, meaty flavor, and blends well with ground beef, chicken, and fish in various proportions. Its chemical composition is as follows: Protein, 17.0 per cent; fat, 2.7 per cent; minerals (ash), 3.0 per cent; water, about 60.0 per cent; and calcium, 0.3 per cent. The content of the B complex vitamins, expressed as micrograms per gram, is as follows: Thiamine, 8.1; riboflavin, 7.1; niacin, 31.1; pantothenic acid, 8.2; and vitamin B_{12}, 0.1. The protein approximates that of medium-fat beef, but its caloric value is only 750 calories per pound, compared with about 1200 calories per pound for medium-fat beef and about 1500 calories per pound for hamburger meat. For the sake of brevity this processed food will be referred to in this article as the *"Sure" food.*

Stability. The canned product has kept well on the shelf in No. 2 cans at room temperature for over two years without any indication of spoilage. After this period the processed food had the same texture, flavor, and palatability as when freshly prepared. The processed Sure food, in ground form, has kept well in a refrigerator for 6 weeks at temperatures of 33 to 35° and will probably keep much longer.

Acceptability. This food has had excellent acceptance both as a meat-extender and meat-substitute in over ten thousand test meals among college students, children in grade and high schools in the United States, among malnourished children in the suburbs of Rome, Italy, among representatives of various U. S. Government agencies, and among civic organizations, in groups as high as 300 to 450.

This food is particularly adaptable for surgi-

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† Preparations are now being made for its commercial production.

cal and convalescent patients, since it is free from the indigestible connective tissue of meats.

As a *meat-substitute.* The following tasty foods have been prepared and well accepted: Patties, croquettes, patties with cooked rice, chile con carne, vegetable hash, mince pie, and polpetto a sugo (an Italian dish).

As a *meat-extender.* The following palatable foods have had excellent acceptance: beefburgers, meat loaves, chile con carne, ravioli, pimento-pickle loaf for cold slicing, chicken loaf, mince pie, barbecued meat balls, chicken and turkey loaves, ham loaves and ham patties, stuffed peppers, and Salisbury steaks.

Estimated Cost. It has been estimated that the cost to the consumer in one-pound cans would be about 20 cents and in ten-pound institution-size cans, 14 to 15 cents.

Protein Value of the Sure Food. From nitrogen retention studies it was found that the proteins in the Sure food are equal to those in beef and equal to 92 per cent of the proteins in dried whole eggs.

Space does not permit giving all the numerous recipes with which we have had success in large-scale cooking, but a few representative ones will be given to show how the Sure food was used as a meat-extender and as a meat-substitute.

The Sure Food as a Meat-extender

Most of the tests on the Sure food as a meat-extender were made on beefburgers, meat loaves, ham loaves, chicken and turkey loaves, and Salisbury steaks. The earlier product had excellent acceptance in burgers among 1420 children in Arkansas grade schools when one pound of the Sure food was added to one pound of ground shoulder clod or hamburger meat, one egg to every pound of mixture, and salt and pepper to taste. The latest product had 100 per cent acceptance among 689 grade school children in Fayetteville, Arkansas. The mixed ingredients were molded into burgers and baked for 20 minutes at 350° F. and either served on hot buns with mustard, pickle, and onions, or were served as barbecued burgers. Among the total of 2109 children, the burgers were accepted as regular meat hamburgers. In the National School Lunch Program dried eggs are given *gratis* and were, therefore, used liberally. We modified some recipes for burgers with less eggs, and without eggs, which reduced the cost but did not impair the palatability; and we added another recipe with a greater proportion of meat.

Beefburgers with the Sure Food

Recipe No. 1	*Recipe No. 2*
1 lb. ground shoulder clod or hamburger meat	1 lb. ground shoulder clod or hamburger meat
1 lb. Sure food	1 lb. Sure food
2 eggs	1 egg
salt and pepper to taste	3 tablespoons skim milk
	1 tablespoon tomato catsup
	salt and pepper to taste

Recipe No. 3	*Recipe No. 4*
1 lb. ground shoulder clod or hamburger meat	1 lb. ground shoulder clod or hamburger meat
1 lb. Sure food	1/2 lb. Sure food
6 tablespoons tomato juice	1/4 cup of water to which are added
4 tablespoons tomato catsup	1 teaspoon salt and a dash of pepper
salt and pepper to taste	2 tablespoons of tomato catsup

Mold into burgers and bake for 20 minutes at 350° F. For small quantities fry in shortening, turning over frequently to prevent burning. Serve on warm buns, toast, or bread with mustard, mayonnaise, pickle, or tomatoes, same as regular hamburgers.

Meat Loaves with the Sure Food

The meat loaves with the Sure food had excellent acceptance in over 2000 test meals among college students, high school students, and among various civic organizations. Most of the acceptances of the meat loaves were obtained when one part of the Sure food to one pound of ground shoulder clod or hamburger meat was used. However, some individual housewives who tried the Sure food in meat loaves preferred to use two parts of ground beef to one pound of the Sure food. The following are the two recipes used:

Recipe No. 1	*Recipe No. 2*
1 lb. ground shoulder clod or hamburger meat	1 lb. ground shoulder clod or hamburger meat
1 lb. Sure food	1/2 lb. Sure food

1 egg, well-beaten
2/3 cup skim milk or whole milk
salt and pepper to taste
1/3 cup finely chopped green pepper
1/3 cup onions, finely cubed*
2 teaspoons Accent® (monosodium glutaminate)
4 tablespoons tomato catsup

1 egg, well-beaten
2/3 cup skim milk or whole milk
salt and pepper to taste
1/3 cup finely chopped green pepper
1/3 cup onions, finely cubed*
1 1/3 teaspoons Accent®
4 tablespoons tomato catsup

* The cubed onions can be substituted by 1 teaspoon of onion salt, in which case the green peppers are increased to 2/3 cup.

Mix thoroughly, transfer to a two-pound loaf pan basted with shortening, and bake in a moderate oven at 350° F. for one hour and 15 minutes, keeping the loaf pan covered with a lid to retain moisture.

Note: For large scale cooking increase the proportions of the recipes according to the number of individuals to be fed. This also applies to the beefburgers and to the following recipes for the Sure food as a meat-substitute.

The composition of the recipes for meat loaves can be varied to suit one's tastes.

Recipe No. 3 for the beefburgers has been used successfully in meat balls with spaghetti and sauce. All the ingredients are thoroughly mixed, rolled into meat balls, sealed by frying in deep fat, and then baked for 20 minutes at 350° F.

One of the most economical and delicious foods prepared with the Sure product is chicken croquettes. The same recipe was also used successfully in chicken loaves, and turkey loaves, substituting the boned turkey for boned chicken.

Chicken Croquettes with the Sure Food

2 lb. ground chicken
1 lb. of the Sure food, ground
1/4 cup of ground peppers
1/3 cup of ground onions
1/3 cup of ground celery
2 eggs
2 cups of chicken broth
2 teaspoons salt
1/3 teaspoon pepper

Mix all ingredients thoroughly, shape into croquettes, roll in cracker meal and fry in deep fat. Serve with creamed sauce and peas.

The meat balls with spaghetti and sauce, the meat loaf (Recipe No. 1), the chicken croquettes, the chicken loaves, turkey loaves, ham loaves and ham patties have had excellent acceptance in the largest and most modern cafeteria in Northwest Arkansas for 6 weeks; and the meat loaf, chicken loaf, and Salisbury steaks have had excellent acceptance in a local restaurant for 12 weeks.

Ham Loaf Made with the Sure Food

9 lb. ground ham*
9 lb. of the Sure food, ground
3 cups tomato catsup
5 cups tomato juice
1 cup chicken broth
1 tablespoon Accent®
1/4 teaspoon garlic
1/4 teaspoon pepper

Bake at 350° for one hour and a half.

The same recipe was used for large ham patties which were baked for one hour at 350°.

Note: Use 1/4 teaspoon Accent for every pound of meat.

Sauce for the Ham Loaf and Ham Patties

1 gallon of ground pineapple
1/3 gallon of water
3 cups sugar
yellow egg shell coloring
about 6 tablespoons cornstarch as paste

* Trimmings and ends.

The ham loaf and ham patties prepared with above recipe had excellent acceptance in the cafeteria referred to above.

Recipe for Salisbury Steaks with the Sure Food

3 lb. ground shoulder clod or hamburger meat
1 1/2 lb. of the Sure food
1 cup tomato catsup
1 1/3 teaspoons common salt
1 1/3 teaspoons onion salt
3/4 teaspoon powdered garlic
1 1/3 teaspoons Accent®
3/4 teaspoon pepper

Mix thoroughly, mold into steaks and cook as desired.

The above recipe for Salisbury steaks has had excellent acceptance in stuffed peppers in the Northwest Arkansas cafeteria.

Sauce Used for Salisbury Steaks with the Sure Food

6 cups tomato juice
2 green peppers, chopped fine
2 onions, cubed fine
2 cloves of garlic
4 tablespoons flour
1 beef bouillon cube
1/4 teaspoon black pepper

Note: It is necessary to use a fatty grade of ground beef to blend well with the Sure food, which is low in fat. Hamburger meat is quite satisfactory, but if a higher grade of ground beef is preferred, use shoulder clod, but not chuck, which is lean beef.

The Sure Food as a Meat-Substitute

The simplest and most readily prepared palatable food is a *patty* with *cooked rice.* The following is the recipe:

To 2 cups of cooked rice add
2 cups of the Sure food and
1 teaspoon of salt

Mold into patties and bake for 20 minutes at 350° F.

Vegetable Hash with the Sure Food

1 onion, finely chopped
1 Irish potato, cubed
2 carrots, grated
1 sliver of celery, finely chopped
salt to taste

Tenderize in water for about 40 minutes, then add one pound of the Sure food and heat for 10 more minutes. This is a highly nutritious low-cost hash with a high protein content, the taste of which resembles very much that of corned beef hash.

In 1950 the Federal Government had a surplus of turkeys which were distributed *gratis* to the state school lunch programs. Consequently, turkey was used in place of chicken in chicken salads. In April of that year the earlier product was used successfully in a chicken salad and served to 170 children in Fort Smith, Arkansas Junior College. Since the latest product can be used just as efficiently in all recipes as the earlier product, the recipe used with the latter food is given as follows:

Chicken Salad with the Sure Food

Solid pack turkey (minced chicken could be used instead)	4 lb.
Sure food	9 lb.
Hard cooked eggs	3 1/2 dozen
Celery	3 bunches, chopped fine
Sweet Pickles	1 pint, chopped fine
Pimentoes	1 cup, chopped fine
Chicken concentrate	1 cup
Salad dressing	2 1/2 cups

The above ingredients were combined as a salad sandwich filler and it made a very delicious salad. None of the children knew that they were not eating the usual chicken salad. In this salad more than 2 parts of the Sure food were used to one part of solid pack turkey.

Another meatless food for which we have had very good acceptance is *croquettes,* using a regular chicken croquette recipe and substituting the minced chicken with the ground Sure food. These croquettes were served and enthusiastically accepted by over 100 managers of the Arkansas School lunch programs at an annual convention in Little Rock, Arkansas. They were also enjoyed and well digested by a group of 18 nursery school children, two to four and a half years of age, their teachers, and their mothers.

One of the best meatless products we have prepared is *chile con carne with pinto beans,* using a regular chile with beans recipe and substituting the ground beef with the Sure food. This chile was accepted as regular meat chile by several hundred college students on the University of Arkansas Campus at Fayetteville and by 80 children in a local parochial school, where each child asked for a second helping.

An Appraisal of the Low Caloric Value of the Sure Food

Obesity may be considered as the number one health problem in the United States. It is estimated that there are 30,000,000 people in this country who are 10 per cent overweight and 15,000,000 who are 20 per cent overweight.[1]

In a recent article, Dr. W. H. Sebrell[2] states that in America today obesity is the gravest known effect of malnutrition. Mortality for overweight people, according to recent estimates, is well above normal at every age and rises with increasing weight.[3,4] As is well

known, obesity is associated with a high mortality from cardiovascular-renal diseases, diabetes, childbirth, and diseases of the liver and gallbladder. Deaths from diabetes are more than three times as common in the obese as in persons of average weight, and death from cirrhosis of the liver among obese men is more than twice as common as among individuals of normal weight in the same age group. The overweight also have an excessive incidence of hernia, urinary impairments, cancer of the endometrium, and some forms of arthritis. Sebrell concludes, then, that among the nation's major nutrition problems, obesity is in one respect unique.

Because of its low caloric value, the Sure food should be particularly useful for overweight patients. Furthermore, because of its low cost, it should be of value in private and state hospitals which have difficulties in balancing their food budgets.

Summary

A new low-cost, high protein, low calorie food is described. It contains defatted soya flour, dry nonfat milk solids, whole wheat, and vegetable shortening. It is supplemented with minerals and vitamins. The protein content is 17 per cent and its caloric value is 750 calories per pound, or about half that of hamburger meat.

It has had excellent acceptance as a meat extender and meat substitute in over 10,000 test meals among students of all ages and in various institutions. It should prove useful in a wide variety of situations.

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Resumen

Un alimento de bajo costo, rico en proteínas y de bajo valor calórico

Se describe un nuevo alimento de bajo costo, rico en proteínas y de bajo valor calórico. Contiene harina de soya desgrasada, los sólidos de la leche descremada, trigo integral y manteca vegetal, además de un suplemento de minerales y vitaminas. El contenido proteínico es de 17 por ciento y el valor calórico es de 750 calorías por libra, o sea la mitad del que tiene la carne de res.

Ha tenido una excelente aceptación como una adición o substituto de la carne en más de 10.000 pruebas de comida realizadas entre estudiantes de todas las edades y diferentes instituciones. Debe probar su utilidad en una gran variedad de situaciones.

Short-Term FEEDING STUDIES IN INFANTS AND CHILDREN *with Certain* SURFACE-ACTIVE AGENTS* *Used In Food Technology:*

ABSENCE OF EVIDENCE OF TOXIC EFFECTS

By EDMOND PRESTON III, M.D., ANDREW D. HUNT, JR., M.D.,† THOMAS F. MCNAIR SCOTT, M.D., and BERNHARD SPUR, PH.D.

THE use of certain nonionic surface-active agents in facilitating the manufacture, packaging, and distribution of various foods has become widespread.[1] That some of these substances may enhance the absorption of fats from the human gastrointestinal tract has been considered for several years, and the results of experimentation in this direction are still divergent, with the feeling being generally held that these substances are of doubtful value as therapeutic agents.[2] However, in spite of the absence of definitely positive evidence as to benefits to be derived from the administration of such materials, they are being used currently as therapeutic adjuncts in both children and adults suffering from various disorders resulting in impairment of fat absorption.[3]

Although many toxicological studies have been performed on both animals and humans, and although the great majority of this work has revealed no harmful effects resulting from either acute or chronic feeding periods,[1,4] a few papers have appeared purporting to demonstrate nonspecific injurious effects in animals when some of the substances were fed in large amounts, i.e., up to 25 per cent of the animals' diet.[5]

It seemed important, therefore, before undertaking any further investigation into the therapeutic value of these agents, to feed them to children over varying periods of time, and to make observations which would indicate whether or not toxic effects occurred.

The substances chosen were Span 60®‡ (sorbitan monostearate), Tween 60®‡ (polyoxyethylene (20) sorbitan monostearate) and Myrj 45®‡ (polyoxyethylene (8) stearate). The plan was to feed these substances to "normal"** infants and children, the amount fed being markedly greater than that which would normally be encountered either in foods or in therapeutic dosage, although not in the amounts reported deleterious in animals.[5] The subjects would then be followed carefully for gross alterations in weight gain, and deviations from normal, in certain laboratory determinations. Since harmful effects, if present, would most probably manifest themselves first in the gastrointestinal tract, the greatest

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* Tween 60®, Span 60®, and Myrj 45®. Kindly supplied by Atlas Powder Company, Wilmington, Delaware.

† Present address: Hunterdon Medical Center, Flemington, N. J., and Dept. of Pediatrics, New York University College of Medicine.

These studies were supported by a grant in aid from the Atlas Powder Company.

‡ Trade mark of Atlas Powder Co.

** Normal = without demonstrable changes in the systems under investigation.

importance was placed on studies of changes in gastrointestinal function. The limitations of this study were realized at its inception, and the objective was only to determine the presence or absence of frankly abnormal values without attempting to analyze the fluctuations that occur within the range of normality.

Materials and Methods

Patients were selected who were clinically free of any illness related to the systems evaluated, except for one patient who was known to be suffering from fibrosis of the pancreas. They were either convalescent hospitalized children, or relatively normal infants being followed in the out-patient department. In the case of the hospitalized subjects, the agents in question were given by the ward nurses with either the morning or noon feeding. The agents were dispensed as follows: *Span 60*® (a white granular substance) was weighed out in papers by the hospital pharmacist in 4-gram lots. These papers were sent to the ward, and the contents of one paper was mixed with the cereal given to the patient for breakfast. *Tween 60*® (a slightly oily substance) was dispensed in bottles, and 20 drops (equivalent of 1 gram) from a standard hospital dropper was added to one formula. *Myrj 45*® (a white viscous liquid) was measured by means of a standard teaspoon, which, when leveled, was found to contain four grams of this substance. This was given in corn syrup to one infant (R.J.) and added to the formula of the other (V.B.). Daily checks were made by one of us as to the adequacy of consumption on the wards. Those followed in the clinic were given the substances by their mothers, and were seen weekly, one week's supply of the agent being dispensed at each visit. These mothers were chosen for the study by virtue of their reliability, their records of good clinic attendance, and of a doctor-patient relationship which bespoke faithful adherence to our instructions.

The following laboratory procedures were performed:

1. Blood counts according to standard techniques. Hemoglobin determined photoelectrically.

2. Routine urinalyses.

3. Pancreatic enzymes were determined by the following methods:

a. Amylase by Bushong's modification of the method of Free and Myers.[6] Normal range: over 20 mg. for infants over 9 mos. of age.

b. Lipase by modification of the method of Cherry and Crandall.[7] Normal value: greater than 10 cc. NaOH required to neutralize the fatty acids formed by the action of 1.0 cc. of duodenal juice on 2 cc. olive oil.

c. Trypsin by the method of Andersen and Early.[8] Normal range: 0.02 cc. of duodenal juice or less, this being the smallest amount causing liquefaction of gelatin.

Duodenal secretions for these analyses were obtained by the intubation of the patients in a fasting state under fluoroscopic guidance. A double-lumened tube was used, making possible the aspiration of gastric contents in order to minimize contamination of duodenal contents with salivary amylase.

4. Stools were collected over a 48-hour period, and analyzed on the basis of dry weight for fat and nitrogen content. The procedures used in estimating total fat, free fatty acids, neutral fat, soaps, etc. were derived from methods described by Van Slyke, Kajdi and Foweather's modification of the method of Saxon.[9]

5. Stools for qualitative tryptic activity were analyzed by the gelatin film technique of Schwachman *et al.*[10], using Eastman radiographic film.

6. Gastrointestinal radiographic studies were performed by Dr. John Hope, radiologist of the Children's Hospital of Philadelphia.

Results

I. *Span 60*®. The agent was fed, in daily dosages of four grams to two children, J.A.J. and J.B.J., for 37 and 32 doses, respectively, the results being tabulated in Tables I and II. Both these children were normal except for tracheotomies of long standing.

In neither subject were there significant alterations in urinalyses or blood counts. The weight changes gave no indication of interferencce with normal growth. The gastrointestinal radiographic studies in J.A.J. and J.B.J. were unchanged during the course of the feeding period. The duodenal enzymes were not altered by the feeding in J.B.J.; no second intubation was performed on J.A.J. because of technical difficulties due to his tracheotomy.

The stool analyses exhibited a rise in total fat excretion in both children. However, it might be pointed out that some of the in-

TABLE I

J. A. J. (In-Patient)
Age 3 3/12 Chronic Subglottic Stricture with Tracheotomy — Span 60®—4.0 Gm./day, 5/15–6/24/51 (37 Doses)

Date	4/26	5/4	5/9	5/13	5/21	5/31	6/11	6/18	6/19	6/20	6/25	7/3	12/21
Day no. of study	0	0	0	0	7	17	28	35	36	37	42	50	6 mos. f.u.
BLOOD COUNTS													
Hgb. in Gm.	12.6				12.8	12.6			13.8			12.4	12.0
RBC in millions	4.09				4.83	4.5			4.37				
WBC in thousands	8.1				8.35	8.2			8.4			8.9	6.9
Neutrophils	47%				25%	55%			49%				51%
Lymphocytes	51%				70%	41%			48%				38%
Eosinophils	2%				3%	2%			2%				3%
Monocytes	0%				2%	2%			1%				2%
Basophils	0%				0%	0%			0%				0%
URINE													
Urine color	Clear				Clear	Clear				Clear		Clear	Clear
pH	5				6	5				5		5	8
Albumin	0				0	0				0		0	0
Sugar	0				0	0				0		0	0
Acetone	0				0	0				0		0	0
WBC per HPF	Occ.				0–2	0–2				0		1–2	0
RBC per HPF	0				0	0				0		0	0
Specific gravity	1.022				1.010	1.002				1.015		1.002	1.026
ENZYMES													
Amylase in mg.			34										
Lipase in cc.			5										
Trypsin in cc.			0.005										
Stool trypsin				Not Done									
STOOL ANALYSIS													
48 HOURS													
Stool appearance				F				F			F		
Weight in Gm.				64.3				48.33			181.14		
Total dry matter in Gm.				14.67				34.77			44.22		
% nitrogen				5.38				5.05			4.40		
Total fat in Gm.				3.85				6.73			13.42		
Neutral fat in Gm.				0.41				2.79			5.11		
Fatty acids soaps in Gm.				1.25				0.39			0.84		
Free fatty acids in Gm.				2.22				3.58			7.47		
X-ray		N					N						
Weight*				36–0	35–4	35–4	35–8	35–8			35–8	35–4	40–8

N = Normal. F = Formed. f.u. = Follow-up.

* Weights within 5 days of date on which they are listed, expressed as pounds-ounces.

TABLE II

J. B. J. (In-Patient)
Age 17 Months Chronic Subglottic Stricture with Tracheotomy Span 60®—4.0 Gm./day, 5/22–6/25/51 (32 Doses)

Date	5/9	5/10	5/16	5/21	5/24	5/31	6/19	6/20	6/25	7/5	2/2/52
Day no. of study	0	0	0	0	3	10	29	30	35	45	6 mos. f.u.
BLOOD COUNTS											
Total dry matter in Gm.	12.4		12.9		12.9	12.9	14.1*			13.1	13.1
RBC in millions	4.2		4.61		3.23	4.07	4.43			4.33	4.69
WBC in thousands	11.8		10.1		12.5	10.0	10.6			11.7	8.9
Neutrophils	26%		75%		19%	22%	31%			29%	61%
Lymphocytes	68%		22%		69%	74%	61%			64%	38%
Eosinophils	1%		1%		6%	2%	4%			5%	1%
Monocytes	4%		2%		5%	2%	3%			2%	0%
Basophils	1%		0%		1%	1%	1%			0%	0%
URINE											
Urine color	Yel. clear		Yel.		Yel. cloudy	Yel. clear	Yel.			Yel. clear	
pH	5		5		6	5	5			5	
Albumin	Trace		Trace		Trace	0	0			0	
Sugar	0		0		0	0	0			0	
Acetone	0		0		0	0	0			0	
WBC per HPF	0		1–2		5–6	Occ.	0			3–4	
RBC per HPF	0		0		0	Occ.	0			0	
Specific gravity	1.032		1.021		1.027	1.030	1.037			1.027	
ENZYMES											
Amylase in mg.			27					29			
Lipase in cc.			7					12.5			
Trypsin in cc.			0.01					0.01			
Stool trypsin					Not Done						
STOOL ANALYSIS											
48 HOURS											
Stool appearance					NN				NN		
Weight in Gm.					54.0				66.9		
Total dry matter in Gm.					7.79				19.26		
% nitrogen					4.20				2.14		
Total fat in Gm.					2.79				5.76		
Neutral fat in Gm.					1.67				2.64		
Fatty acids soaps in Gm.					0.57				0.60		
Free fatty acids in Gm.					0.54				2.52		
X-ray		Norm.							Norm.		
Weight†		23–0		22–8		22–4	23–8		23–0	22–0	34–12

NN = Not noted. f.u. = Follow-up.
* Had been placed on oral iron 6/6/51 (16th day of study).
Weights within 5 days of date on which they are listed, expressed as pounds-ounces.

Weights within 5 days of date on which they are listed, expressed as pounds-ounces.

TABLE III

V. B. (Out-Patient)
Age 10 Months Feeding Problem

Tween 60®—1.0 Gm./day, 8/6–9/5/51 (31 Doses)
Myrj 45®—4.0 Gm./day, 9/10–9/24/51 (14 Doses)

Date	7/26	7/28	8/6	8/13	8/20	8/27	9/4	9/6	9/10	9/12	9/17	9/24	9/26	1/5/52
Day of feeding (Tween 60)	0	0	0	8	15	22	30	32	36	38	43	50	52	4 months
Day of feeding (Myrj 45)	0	0	0	0	0	0	0	0	0	2	7	14	16	follow-up
BLOOD COUNTS														
Hgb. in Gm.	11.7			10.0	10.0	11.8	10.7		10.8			11.3		10.3
RBC in millions	3.96			3.52	4.15	4.78	3.92		4.13			4.5		4.2
WBC in thousands	7.75			9.1	9.1	11.05	7.1		7.5			8.05		6.45
Neutrophils	29%			46%	30%	25%	31%		29%			17%		65%
Lymphocytes	71%			49%	66%	74%	68%		68%			70%		32%
Eosinophils	0%			1%	0%	0%	1%		1%			5%		2%
Monocytes	0%			2%	4%	1%	0%		0%			8%		1%
Basophils	0%			0%	0%	0%	0%		2%			0%		0%
URINE														
Color			Y. clear									Y. clear		
pH			6									5		
Albumin			0									0		
Sugar			0									0		
Acetone			0									0		
WBC per HPF			1–2									8–10		
RBC per HPF			0									0		
Specific gravity			1.022									1.018		
ENZYMES														
Amylase in mg.										10.0			7.4	
Lipase in cc.										17.0			4.5	
Trypsin in cc.										0.01			0.01	
Stool trypsin		Pos.		Pos.			Pos.							
STOOL ANALYSIS														
48 HOURS														
Stool appearance		F.		F.			F.					SS		
Weight in Gm.		75.3		57.3			46.6					8.5		
Total dry matter in Gm.		16.9		26.8			13.5					2.5		
% nitrogen		3.5		2.5			4.0					3.8		
Total fat in Gm.		4.5		6.0			4.6					1.2		
Neutral fat in Gm.		1.8		2.1			1.9							
Fatty acids soaps in Gm.		1.2		2.5			1.4							
Free fatty acids in Gm.		1.6		1.5			1.3							
X-ray			A					A				N		
Weight	15–12		16–1	16–1	16–9	16–8	17–0		17–4		17–9		17–0	18–5

SS = Semi-Solid. A = Abnormal—see comment. F = Formed. N = Normal. Y. Clear = Yellow clear.

TABLE IV

V. S. (Out-Patient)
Age 8 Months Premature Twin

Tween 60®—1.0 Gm./day, 8/6–9/8/51 (34 Doses)

Date	7/26	8/2	8/6	8/13	8/20	8/27	9/4	9/10	9/19	9/20	9/21	9/24	2/2/52
Day no. of study	0	0	1	8	15	22	30	36	45	46	47	50	4 mos. f.u.
BLOOD COUNTS													
Hgb. in Gm.	10.00			9.8	9.8	10.4	10.0	10.9	10.0				10.4
RBC in millions	3.60			3.99	4.02	4.77	4.33	4.25	4.06				3.94
WBC in thousands	13.1			10.0	8.4	12.15	11.5	6.1	7.9				10.8
Neutrophils	40%			32%	38%	28%	31%	33%	37%				49%
Lymphocytes	60%			64%	58%	68%	63%	56%	54%				50%
Eosinophils	0%			2%	2%	1%	1%	5%	6%				1%
Monocytes	0%			2%	1%	3%	4%	2%	3%				0%
Basophils	0%			0%	1%	0%	1%	2%	0%				0%
URINE													
Urine color										Yel. cloudy			
pH										5			
Albumin										0			
Sugar										0			
Acetone										0			
WBC per HPF										0			
RBC per HPF										0			
Specific gravity										1.020			
ENZYMES													
Amylase in mg.											10.0		
Lipase in cc.											7.0		
Trypsin in cc.											0.02		
Stool trypsin			Pos.		Pos.		Pos.						
STOOL ANALYSIS 48 HOURS													
Stool appearance			F.		F.		F.						
Weight in Gm.			61.4		32.3		46.0						
Total dry matter in Gm.			32.44		6.33		11.55						
% nitrogen			3.63		3.33		3.86						
Total fat in Gm.			8.31		2.37		5.72						
Neutral fat in Gm.			0.96		0.14		2.44						
Fatty acids soaps in Gm.			5.59		1.24		2.17						
Free fatty acids in Gm.			1.76		0.99		1.09						
X-ray		N								N			
Weight	14–15		15–7	16–1	15–12	15–15	16–7	17–0	18–9	18–6	18–6	18–12	24–12

N = Normal. F = Formed.

TABLE V

TABLE V

J. S. (In-Patient)
Age 11 Months Convalescent after Edema from Acute Salt Retention Tween 60®—1.0 Gm./Day, 10/8–10/21/51 (13 Doses)

Date	10/5	10/8	10/9	10/12	10/13	10/15	10/16	10/17	10/20	10/21	10/22	10/23	10/24	4/28/52
Day no. of study	0	1	2	5	6	8	9	10	13	14	15	16	17	6 mos. f.u.
BLOOD COUNTS														
Hgb. in Gm.		6.3*		7.5				9.5		10.0			10.7	Unable
RBC in millions		3.65		3.07				3.84		4.61			4.50	to
WBC in thousands		12.9		8.0				5.4		6.8			6.9	locate
Neutrophils		28%		32%				35%		18%			28%	for
Lymphocytes		71%		66%				63%		79%			57%	follow-up
Eosinophils		0%		0%				1%		2%			5%	
Monocytes		1%		2%				0%		0%			9%	
Basophils		0%		0%				1%		0%			0%	
URINE														
Urine color	Colorless				Sl.–cloudy yellow			Colorless	Yel. clear				Yel. cloudy	
pH	7				5			5	6				6	
Albumin	0				Very ft. trace			0	0				Slt. trace	
Sugar	0				0			0	0				0	
Acetone	0				0			0	0				0	
WBC per HPF	3–5				Occ.			0	0				1–2	
RBC per HPF	0				0			0	0				0	
Specific gravity	1.010				1.014			1.012	1.012				QNS	
ENZYMES														
Amylase in mg.			16.0									17.4		
Lipase in cc.			12 1									2.0		
Trypsin in cc.			.01									0.02		
Stool trypsin					Not Done									
STOOL ANALYSIS 48 HOURS														
Stool appearance			SS				SS					SS		
Weight in Gm.			211.6				49.7					137.10		
Total dry matter in Gm.			35.67				17.57					36.42		
% nitrogen			3.06				3.29					3.06		
Total fat in Gm.			11.95				7.69					11.73		
Neutral fat in Gm.			0.02				0.17					0.49		
Fatty acids soaps in Gm.			6.28				5.40					6.78		
Free fatty acids in Gm.			5.65				2.12					4.46		
X-ray			NS			PN					N			
Weight†	17–15			18–12		18–8		18–9		18–10			19–5	

* Given 150 mg. Feojectin® I.V. (10/6–10/8).
† Weights within one day of date on which they are listed, expressed as pounds-ounces.
N = Normal. NS = Not satisfactory. PN = Probably normal. f.u. = Follow-up.

TABLE VI

E. H. (In-Patient)
Age 6 Months Mucoviscidosis

Tween 60®—1.0 Gm./day, 10/8–10/20/51 (12 Doses)

Date	10/6	10/9	10/11	10/12	10/13	10/18	10/19	10/22	10/24	10/26	11/19/51
Day no. of study	0	2	4	5*	6	11	12	15	17	19	1 mo. f.u.
BLOOD COUNTS											De-
Hgb. in Gm.	11.0			11.7		12.0		11.8	11.3		ceased
RBC in millions	4.58			4.0		3.98		4.18	3.89		this
WBC in thousands	32.5			20.0		16.4		8.2	13.7		date
Neutrophils	71%			54%		60%		73%	51%		
Lymphocytes	24%			45%		40%		23%	45%		
Eosinophils	0%			0%		0%		2%	0%		
Monocytes	5%			1%		0%		2%	4%		
Basophils	0%			0%		0%		0%	0%		
URINE											
Urine color	Pale yel.				Yel. clear	Yel. clear		Yel. cloudy	Yel. clear		
pH	7				5	5		7	5		
Albumin	0				F. trace	0		Trace	0		
Sugar	0				0	0		0	0		
Acetone	0				0	0		0	0		
WBC per HPF	Occ.				8–10	1–2		Occ.	0–1		
RBC per HPF	0				Occ.	0		0	0		
Specific gravity	1.005				1.022	QNS		1.020	1.004		
ENZYMES											
Amylase in mg.			0.7					1.2			
Lipase in cc.			0					0.15			
Trypsin in cc.			0					0			
Stool trypsin					Not Done						
STOOL ANALYSIS											
48 HOURS											
Stool appearance		SS							Soft		
Weight in Gm.		194.0							49.2		
Total dry matter in Gm.		47.03							15.34		
% nitrogen		6.32							8.62		
Total fat in Gm.		29.21							4.35		
Neutral fat in Gm.		7.17							0.77		
Fatty acids soaps in Gm.		3.05							1.07		
Free fatty acids in Gm.		18.99							2.51		
X-ray		Normal					NS				
Weight†	10	10–3		9–6	9–12	9–9		9–14	10–3	9–15	10–5

SS = Semi-solid. F. trace = Faint trace. NS = Not Satisfactory.

* Started on Pancreatin 1.0 Gm. q.i.d.

† Weights within two days of date on which they are listed.

TABLE VII

R. J. (In-Patient)
Age 6 Years Dwarfism of Unknown Etiology Myrj 45®—4.0 Gm./day, 9/8–9/24/51 (16 Doses)

Date	8/10	8/13	8/15	8/17	9/7	9/14	9/15	9/19	9/21	9/22	9/24
Day of study	0	0	0	0	0	7	8	12	14	15	18
BLOOD COUNTS											
Hgb. in Gm.	10.4					10.9				10.4	
RBC in millions	3.4					3.3				3.5	
WBC in thousands	4.7					8.15				11.0	
Neutrophils	27%					32%				40%	
Lymphocytes	62%					41%				49%	
Eosinophils	7%					6%				6%	
Monocytes	4%					1%				0%	
Basophils	0%					0%				1%	
URINE											
Urine color	Clear					Clear				Clear	
pH	8					5				6.5	
Albumin	Trace					F. trace				0	
Sugar	0					0				0	
Acetone	0					0				0	
WBC per HPF	0					5–6				Occ.	
RBC per HPF	Occ.					0				Occ.	
Specific gravity	1.017					1.032				1.021	
ENZYMES											
Amylase in mg.			26					29			
Lipase in cc.			2.6					10			
Trypsin in cc.			0.005					0.02			
Stool trypsin		Pos. 1:100									
STOOL ANALYSIS 48 HOURS											
Stool appearance							SS			GSS	
Weight in Gm.							138.0			247.0	
Total dry matter in Gm.							27.1			82.8	
% nitrogen							8.4			7.4	
Total fat in Gm.				4.2			7.35			9.3	
Neutral fat in Gm.				(24 hrs.)			1.65			0.48	
Fatty acids soaps in Gm.							2.51			2.16	
Free fatty acids in Gm.							3.19			6.67	
X-ray				N					N		
Weight					33–0	33–4				33–8	34–4

SS = Semi-solid. GSS = Greenish semi-solid. F. trace = Faint trace. N = Normal.

creased fat might have been due to the unabsorbed stearic acid from the Span®. In both children the highest level was either well within (J.B.J.) or at upper limit (J.A.J.) of generally considered normal values.

II. *Tween 60®*. This emulsifying agent was given in a daily dosage of one gram, to three normal or slightly malnourished children (V.B., V.S., J.S.) and one child (E.H.) suffering from mucoviscidosis. The data are summarized in Tables III, IV, V, and VI, respectively.

As in the cases of the children given Span 60®, there was no effect on blood counts or urinalyses in these subjects.

In the patients V.B. and V.S., both of whom were out-patients, a duodenal intubation prior to the starting of the feeding of Tween 60® was not performed. However, the duodenal enzymes after the feeding period in V.S. were within normal limits for infants of this age. Trypsin was demonstrated in the stools at intervals during feeding in both children. In patient J.S. intubations were performed both on the 2nd and 16th day of the feeding of Tween 60®, and the results were not abnormal. The change in lipase activity is probably not of significance, since the results of estimation of this enzyme are known to be notoriously variable. Patient E.H. showed the absence of duodenal enzymes characteristic of mucoviscidosis. This diagnosis was confirmed at autopsy, a few months after the conclusion of the study. In none of the children was weight gain apparently affected by feeding the emulsifying agent, Tween 60®.

The gastrointestinal radiographic series in the case of patient V.B. showed some hypomotility and "puddling" on two occasions. This was observed prior to the feeding of Tween 60®, and probably represented a normal variant in view of normal stools, good weight gain, and an entirely normal study at the end of the feeding periods of Tween 60® and Myrj 45® (see below). In the three normal infants, V.B., V.S., and J.S., there was no alteration of fecal fat moieties of any significance. The marked fall in stool fat content in patient E.H. was the result of the low fat diet prescribed for her basic disease.

III. *Myrj 45®*. This agent was given to two patients in doses of four grams daily. One of these patients (R.J.) was a 6-year-old boy who was suffering from dwarfism of unknown etiology and weighed only 33 pounds. The second patient (V.B.) had previously been given Tween 60® (see above). The Myrj® feeding was not begun until an interval of 7 days had elapsed after cessation of the Tween 60® feeding.

The data are tabulated in Tables VII and III respectively. It can be seen that as with Span 60® and Tween 60® there were no significant changes in the blood counts, urine analyses, or weight progress. The slight drop in weight in V.B. on September 26, 1951, two days after cessation of the feeding, could be explained by the fact that her weight on this occasion was obtained after she had been intubated, so that environmental circumstances were not the same as at the time of her first and second weights.

The only change in the duodenal enzymes in R.J. was a rise in lipase to the normal range after 12 days of Myrj 45® feeding. Two intubations were done on V.B. in relation to the Myrj 45® feeding. One on the second day of feeding was normal for lipase and trypsin and slightly low in amylase. The second test, two days after cessation of feeding, showed a drop in lipase with no significant changes in the other two. Since considerable variation occurs in amylase and lipase in normal infants, it is difficult to ascribe the changes found to the administration of Myrj 45®.

The second stool on V.B. probably did not represent a true 48-hour collection, judging by the wet weight, but the percentages of fat in the previous stool and this one were 33.9 and 46.9, respectively. There were no significant changes in the nitrogen or total fat excretion in the stools following feeding this material in either of these children.

Summary and Conclusions

1. Sorbitan monostearate (Span 60®) was fed to two children, in dosage of four grams daily for 37 doses in a period of 41 days and 32 doses in a period of 35 days, respectively.

2. Polyoxyethylene (20) sorbitan monostearate (Tween 60®) was fed to three infants in dosage of one gram daily as follows: 31 doses in 31 days, 34 doses in 34 days, and 13 doses in 14 days, respectively. The substance was also fed in the same dosage of 12 doses in 13 days to one infant of 6 months, who was suffering from mucoviscidosis.

3. Polyoxyethylene (8) stearate (Myrj 45®) was fed to two subjects in dosage of four grams daily for periods of 16 days and 14 days, respectively.

4. No harmful effects, as reflected in behavior, general health, appetite, frequency or consistency of stools, or weight gain were noted in the "normal" children. A follow-up in four of these children, 4–6 months after the conclusion of the study, showed them to be progressing normally, and with normal blood counts. The patient with mucoviscidosis died and the diagnosis was confirmed at autopsy.

5. No gross laboratory evidence of toxicity from these substances, as reflected in blood counts, urinalyses, pancreatic enzymes, gastrointestinal radiographic studies, or quantitative analyses of stools for fats and nitrogen, were observed in the "normal" children, and no change for better or worse in the patient with mucoviscidosis.

Addendum

As a supplement to the acute feeding studies described above, investigations were carried out by Dr. Bernhard Spur on the *in vitro* effect of Tween 60® on the action of the proteolytic enzymes of gastric juice. The chief enzyme here is *pepsin,* which acts optimally at a pH of between 1.0 and 2.0. There is further action between pH of 3 × 7.4 which is outside the generally considered range for pepsin, and may indicate the presence of cathepsin. The technique used was as follows:

The gastric juice was obtained from babies in the morning before any meals had been given, and the pH of the gastric juice was measured before the testing of its digestive activity. The digestive activity of the gastric juice was tested on skim milk, which was placed in rubber bags, each containing 100 ml. milk. These bags were suspended in a special water bath, where they could be agitated slightly during the digestion period by a special mechanical device. The temperature of the water in the water bath was 37° C. To each 100 ml. milk, 5 ml. gastric juice was added. Tween 60® was added to some to a final dilution of 1–2 per cent. The pH was then adjusted by the addition of hydrochloric acid to the optimal level suited for the enzyme being studied. For "cathepsin," the pH of the milk-gastric juice mixture was adjusted to about 4, and for pepsin to about 2.

The digestion time was 2½ hours, which is the time milk normally stays in the stomach of a healthy child. After digestion, during which the milk coagulates, the whey was filtered from the coagulate and the nitrogen content was measured by Kjeldahl's method.

Controls consisting of the milk alone were processed in the same way at the corresponding levels of pH, and the nitrogen content of the whey of these specimens was determined. The amount of soluble nitrogen in the whey after digestion in excess of what was present in the control, indicated the digestive

TABLE VIII

Digestion of Milk with Gastric Juice, With and Without Addition of Tween

Case No.	Tween	N in Whey	N in Milk	Total Protein Digested
	%	%	%	%
Gastric Juice at pH 3.7–4.0 ("Cathepsin")				
1	—	0.0292	0.522	6.5
	1	0.0332		7.5
3	—	0.121	0.529	28.9
	—	0.124		29.7
	1	0.111		26.6
5	1	0.032	0.523	7.2
	1	0.042		9.5
	2	0.027		6.1
	2	0.033		7.5
	—	0.025		5.7
6	1	0.180	0.520	39.8
	2	0.182		40.0
	—	0.181		39.9
Gastric Juice at pH 1.0–2.0 (Pepsin)				
2	—	0.137	0.509	27.0
	1	0.139		27.3
4	1	0.199	0.495	47.0
	1	0.205		48.0
	2	0.217		50.0
	2	0.217		50.0
	—	0.215		49.0
	—	0.221		52.0
7	1	0.216	0.520	50.0
	2	0.225		52.1
	—	0.250		57.8

activity of the enzyme. A nitrogen determination was also performed on the whole skim milk; from this the proportion of the total protein in the milk that had been digested by each enzyme could be calculated.

The results given in Table VIII indicated that there was no constantly reproducible effect on protein digestion *in vitro* by the addition of Tween 60® to the gastric juice-milk mixture at either pH range.

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Resumen

Estudios de cortos períodos de alimentación realizados en niños con ciertos agentes de superficie utilizados en tecnología alimenticia: ausencia de evidencia de efectos tóxicos

Dos niños fueron alimentados con monoestereato de sorbitan (Tween 60) con una dosis de 4 gramos diarios por 37 dosis en un período de 41 días y 32 dosis en un período de 35 días, respectivamente.

Monoestearato polioxietileno de sorbitan (Span 60) se administró a tres infantes en dosis de un gramo diario en la siguiente forma: 31 dosis en 31 días, 34 dosis en 34 días, y 13 dosis en 14 días, respectivamente. Esta substancia se administró también en la misma dosis, 12 dosis en 13 días, a un infante de 6 meses que padecía de mucoviscidosis.

Estearato de polioxietileno (8) (Myrj 45) se administró a dos sujetos en dosis de 4 gramos diarios, por períodos de 16 y 14 días, respectivamente.

No se observaron efectos nocivos que podían reflejarse en la conducta, salud general, apetito, frecuencia y consistencia de las materias fecales, ganancia de peso, etc. en los niños "normales." A cuatro de estos niños se les observó por un período de 4 a 6 meses después de la terminación de los estudios y todos mostraron progresar normalmente y con recuentos globulares normales. El paciente con mucoviscidosis murió y el diagnóstico fué confirmado por la autopsia.

En los niños "normales" los estudios de laboratorio no revelaron evidencia de toxicidad de estas substancias que podían reflejarse en los recuentos globulares, exámenes de orina, enzimas pancreáticas, estudios radiográficos gastrointestinales o análisis cuantitativas para grasas y nitrógeno en las materias fecales. En el niño afecto de mucoviscidosis no se observó ningún cambio significativo.

Editorial

The Oral Tissues and Nutrition

The importance of nutrition in everyday diagnostic and therapeutic procedures is generally recognized by the physician. Nevertheless, the significance of changes in the oral tissues in early nutritional disturbances and the importance of diseases of the oral tissues in the production of "conditioned deficiencies" deserve increased consideration by the physician.

The control of dental caries, the most important dental disease in the child and adolescent, can be effectively achieved by adequate diets low in fermentable carbohydrates. A more general appreciation of the role of fermentable carbohydrates in the initiation of dental caries by the family physician and pediatrician would make obsolete the all too common practice of lollypop prizes for good behavior.

Changes in the lips, in the color of the oral mucosa, and in the tongue coating are sensitive indicators of systemic disturbances among which nutritional disorders are most common. A thorough understanding of the appearance of the oral tissues in health is essential for the correct interpretation of abnormal findings in these structures. Due to the peculiar environment of the oral tissues, these mucosal and lingual changes may exist long before the more severe and characteristic signs and symptoms appear in other parts of the body.

The uncommon and spectacular gingival changes in acute scurvy are readily recognized, but the slight cheilitis, the abnormal redness and opalescence of the buccal mucosa, and the tongue changes in early vitamin B complex deficiency are often overlooked, as are the oral changes associated with undiagnosed diabetes mellitus.

The patient with periodontal disease (pyorrhea) is not only unable to adequately prepare the food for efficient digestion but the transient bacteremias associated with periodontal disease and the continual swallowing of potentially infectious material may initiate or aggravate already existing disease in more distant parts of the body.

Artificial dentures *per se* by no means assure an adequate masticatory apparatus. The efficiency of the best artificial dentures is approximately only 25 per cent of the natural dentition, and far too many artificial dentures serve mainly an esthetic or cosmetic purpose. Too often mild nutritional deficiency states prevent proper functioning of well constructed artificial dentures because of the lowered resistance of the denture supporting mucosal tissues.

An adequately functioning, healthy chewing apparatus is particularly important in the geriatric patient. Many nutritional problems in older persons are indirectly related to inadequate preparation of the food in the mouth or a poorly balanced "convenience" selection of high carbohydrate diets because of faulty functioning dentures.

The oral tissues and nutritional disturbances are mutually inter-related. The significance of diseases of the oral structures as important factors in the production or accentuation of nutritional problems is well recognized by the specialist in nutritional problems, but it is the general practitioner who should strive to recognize these lesions in their early, more reversible stages. A greater appreciation of the oral tissues in health and disease is needed for the early recognition and effective treatment of nutritional disturbances and oral disease.

—Lester W. Burket, D.D.S., M.D.

Dietotherapy

MAN, HIS NUTRITION, AND HIS YEARS

By VERA W. WALKER, M.S.*

"THAT THY YEARS may be long upon the land which the Lord thy God giveth thee" has been the rosy prospect held forth as the reward for following any number of patterns of eating, of medication, or of living since the beginnings of recorded history. The relation of diet to longevity has been pointed out repeatedly through the years, but the recommendations have often been at variance.

Luigi Cornaro,[1] who lived for a century, or thereabouts, and died in 1566, wrote that "between his 35th and 40th year, his infirmities were very great because he had been intemperate in the matters of eating and drinking. He had enjoyed great wealth and had no reasons to be frugal in his ways of living." But when he was warned that his days were numbered, but might be lengthened somewhat if he adopted a sober and well regulated life, he reformed, and became firmly convinced that it was on this account that he lived to a mellow old age. His advice was, "Oh how advantageous it is for an old man to eat but little; therefore I take but just enough to keep body and soul together, and the things I eat are as follows: bread, panado, eggs (the yolk), and soups. Of flesh meat I eat kid and mutton. I eat poultry of every kind; also of sea and river fish. Some men are too poor to allow themselves food of this kind, but they may do well on bread (made from wheat meal, which contains far more nutriment than bread made from fine flour) panado, eggs, milk, and vegetables. But though a man should eat nothing but these, he may not eat more than his stomach can with ease digest, never forgetting that it is the over quantity which injures, even more than the eating of unsuitable food."

Some one hundred years later, Bacon[2] was just as firmly convinced that "Diet well ordered bears the greatest part in the prolongation of life. . . . Curing of Diseases is effected by Temporary Medicines but Lengthening of Life requireth observation of Diets." Allen[3] wrote, in 1840, that "It cannot be denied that a difference in diet will produce a corresponding difference in the health and constitution of different people. This is acknowledged by all who have paid attention to the effects which a peculiarity of diet is capable of producing. . . . We cannot imagine that man can be reformed solely by attention to dietetic rules as some have imagined; yet we are fully convinced that if men would return more nearly to their pristine state of living, as regards their food, it would have a tendency to make them longer lived, and to elevate them in the scale of moral and intellectual beings." He also lamented our modern methods of mangling food by ten thousand operations of cookery for the express purpose of pleasing the appetite and encouraging people to eat twice as much as they should!

French,[4] too, some fifty years later, believed that "The first necessity of age as of youth is food; but errors in diet are specially harmful now. The young man has a reserve of vitality to draw upon . . . but the old man's bank account is already overdrawn and he is living from hand to mouth. . . . He must therefore carefully measure his digestive power, and adapt his food, both in quantity and kind, to the needs of his system." He philosophizes

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that "Some misguided enthusiasts have believed that by lengthening life they would confer a priceless boon on the human race; forgetting that it is not the length of day which makes us love the summer but the brightness of the sun, the beauty of the flowers, and the singing of the birds."

Today, we are still concerned with a "way of keeping people young as they grow old—not young in years but young in the sense that we associate energy, usefulness, and creativity with youth. This is our key problem. . . . Nathaniel Bacon was only 29 when he revolted against colonial rule in Virginia; but Benjamin Franklin was 81 when his tact, tolerance, and mental elasticity saved the Constitutional Convention. Keats died before he was 26; but Titian painted his 'Crowning with Thorns' at 95. The calendar alone has never been a good gauge of productive capacity in any individual man or woman."[5]

Modern dietary recommendations for a long and useful life are not far different from those of Cornaro, but the bases for our recommendations have greater scientific weight. Animal studies of longevity have obviously been more feasible than studies with human beings. Among these, the observations of Sherman and co-workers[6] have become classic. These began with the observation that laboratory rats on an adequate stock diet lived average lives satisfactory for stock animals, but that by increasing the proportion of dry whole milk in the stock diet from one-sixth to one-third, the animal's life span was increased by ten per cent, but more significantly, adult vitality was maintained at a higher level for a considerably longer time. It is, of course, the hope of prolonging the period in which we maintain the characteristics of youth which is the goal of most dietary research. McCay and co-workers[7] have also contributed a series of studies on longevity in which it was shown that restriction of calories was the most important single factor.

Calories

There is general agreement today that McCay's observations that lean rats live longest are probably applicable to human beings as well. Life insurance company tables of "normal" and recommended weights for adults have been scaled downward in recent years as a result of studies of the association of overweight with the incidence and mortality of the degenerative diseases.[8] Jolliffe[9] has summarized the data: "In both men and women, death rates for the overweights were well above normal at every age, and when all ages were grouped together they amounted to 150 per cent for men and 147 per cent for the women. . . . Except in very unusual circumstances, people are not listed as dying of obesity. The death from obesity will be found hidden in the figures of heart disease, high blood pressure, arteriosclerosis, kidney disease, diabetes, and cancer, which are not only the leading causes of death but are, in addition, the diseases in which the death rates are increasing." A recent reviewer[10] has put it: "The case against obesity from the point of view of chronic disease is overwhelming: the increased incidence of diabetes mellitus, and of cardiovascular-renal disease, the possibility of accentuating hypertension and accelerating the appearance of arteriosclerosis, the tendency to bring on hypertrophic arthritis, the added pain in rheumatoid arthritis, and the increased tendency for accidents are points which are emphasized in day to day experience with obese patients."

The bases for the tendency toward overweight which is seen in many older adults are probably numerous. The lowering of basal metabolic rate by some 10 to 15 per cent in mature adults has long been recognized. There is usually a slackening of physical pace also, which lowers the need for calories still further. Unfortunately, there is not always a decrease in appetite to accompany the decrease in need for calories. With the loss of teeth and the dulling of taste sensitivity, there may be a tendency to eat softer, more bland foods, which often have more calories in relation to their volume than do the fruits and vegetables which they tend to replace. Much has been written of the psychological factors of overeating as compensation for unmet emotional needs. Thewlis[11] lays part of the blame for obesity in older persons on their children and

relatives, who overfeed them as a demonstration of their care and affection. "It would be far kinder," he adds, "to restrict the diet, to urge them not to overeat, and if necessary, to buy only a minimum of food."

The amount of decrease in caloric need appears to vary with individuals, probably remaining higher in people who maintain their health and vigor.[12] Keys[13] suggests a reduction in basal metabolism of five per cent for each decade beyond 50 years, with an additional reduction for lessened physical activity. He states that older women often maintain their health and vigor on 1500 calories or less, while older men require 2000 calories or less. He adds that there should be a gradual weight loss with advancing years; for if the weight is the same at 70 as it was at 40, there has been a replacement of muscle tissue by fat. FAO studies[14] recommend a calorie reduction of 7.5 per cent for each decade above 25 years. Thus the requirement at 35, 45, 55, and 65 would be 92.5, 85, 77.5, and 70 per cent, respectively, of the calorie requirement for that individual at 25 years.

It seems advisable that most of the reduction in calories should come from a reduction in the amounts of fat and carbohydrates consumed. The role of dietary fat in the deposition of cholesterol in arterial walls is still under investigation, but fats are often a cause of indigestion, perhaps because of a reduction in gastric, liver, and pancreatic activity. Obviously, what fats are used for flavor and satiety value should be largely those which carry vitamins A and D. Older people are said to have a reduced capacity to maintain stable blood sugar levels, and so are more subject to temporary hypo- or hyperglycemia than are younger people. The precise impairment (of liver, pancreas, or muscle tissue) responsible for this retardation is not clear,[15] but the use of sugar may well be restricted to prevent an undue load on the sugar-regulating mechanism of the body. Starchy foods are mobilized and burned more slowly than sugar; and in many instances starchy foods (such as whole grain or enriched cereals, potatoes, and dried beans) carry B-vitamins, iron, or other necessary food elements which give them distinct nutritional advantages over purified sugars.

Proteins

In McCay's studies[7] the group of rats which lived longest was given a diet containing eight per cent protein in the form of liver, had its calories restricted, and was given enforced exercise daily. Not all human beings would wish to be long-lived on that routine. In fact, few older women on self-selected diets eat liver more than once a month.[16]

One of the characteristics of aging commonly considered to be "normal" is a gradual decrease in muscle volume and in size of some of the organs.[15] Negative nitrogen balances of greater or less degree are often found when balance studies of older persons are made, and clinical protein deficiencies are frequently seen.[17,18] Such deficiencies contribute to anemia, edema, and tissue wastage. Dietary studies of older persons frequently show low intakes of the foods which are good sources of protein.[16,19,20] Reduced gastric hydrochloric acid is to be expected in older persons, and achlorhydria is seen in some 35 per cent of the population above the age of 60.[15] The question arises as to whether the protein deficiencies seen are due solely to low intake or to a combination of low intake plus incomplete digestion and assimilation.

Whatever the causes of negative nitrogen balances and of apparent protein deficiencies, a number of studies have shown that older persons can be kept in balance on intakes of 0.7 to 1.0 Gm. protein per Kg. of body weight per day[12,21,22] when extended over a long period of time, although it may be necessary to give 1.0 to 2.0 Gm. per Kg. to obtain positive nitrogen balances in some individuals.[17,22] Kountz *et al.*[22] found, however, that their subjects, even though they made an effort to cooperate, could not tolerate more than 1.0 to 1.5 Gm. protein per Kg. over a prolonged period.

The need for adequate protein of good quality in the diets of older people is being given increased emphasis. The relation of protein to certain other conditions related to aging has been reported. The development of a strain

of black mice which is subject to joint changes resembling human rheumatoid degenerative arthritis has made possible studies of nutrition in relation to that condition. Silberberg and Silberberg[23] have found that when mice of this strain were given high protein diets throughout life, there was a reduced incidence of the arthritis, and a higher per cent of normal joints at any age. The osteoporosis which is so frequently seen in older persons may also be related to protein, as well as to calcium and other factors. According to Albright and Reifenstein,[24] "it is proposed that osteoporosis is characterized by a defective synthesis of protein matrix which prevents replacement of bone lost in the course of usual metabolic turnover." Morgan[25] has reported that atopic dermatitis and eczematous or senile pruritis seen in patients over 60 years of age almost always clear up when the patient is given increased amounts of protein foods and supplementary amino acid powders.

Vitamins and Minerals

Sherman, in his studies of longevity in laboratory animals, found that it was vitamin A and calcium which made the significant difference between the merely adequate diet and the diet which promoted longer, more vigorous life. In humans, Ohlson *et al.*[16] found that women with "adult vitality," who were healthy, vigorous, and interested in community activities, ate much more of the foods which are good sources of minerals and vitamins than did other groups of similar ages who had poor health.

A number of studies have shown that increases in vitamin intakes give improvement in general vitality and vigor, and/or improvement in specific conditions commonly associated with deficiency in certain vitamins. Stephenson *et al.*[26] claimed to have found improvement in general health and vigor when a group of older persons was given B-vitamins and vitamin C. Jolliffe,[27] Kyhos *et al.*,[28] and others have found that it often takes large doses of the water-soluble vitamins to saturate elderly patients with deficiencies of long standing.

Kirk and Chieffi[29] have studied the effects of prolonged administration of vitamin A on older people who had certain conjunctival lesions, blepharoconjunctivitis, slow dark adaptation, and follicular hyperkeratosis. These conditions were found in a group of institutionalized persons who had access to a diet providing 10,000 I.U. of vitamin A daily. A significant reduction of these conditions was obtained after four to ten months of treatment with 30,000 I.U. daily of a water-soluble dispersion of vitamin A preparation. The fact that these conditions developed when the diet appeared to be adequate in vitamin A, and disappeared with the prolonged use of a water-soluble dispersion of the vitamin may be related to the low gastric acidity and poor fat absorption so frequently seen in older persons. It should be noted, also, that some of the lesions which improved with vitamin A administration are frequently seen in older adults, and are often thought to be "normal" characteristics of aging.

Mild niacin deficiency is not uncommon in older persons, as evidenced by a smooth, red tongue, with or without digestive disturbances or skin changes suggestive of pellagra. The patient may become stuporous or disoriented and confused, and may have hallucinations, cogwheel rigidity, and sucking reflexes.[18] Gregory[30] has recently emphasized the importance of maintaining normal niacin blood levels as prophylaxis against the "psychoses of senility," since a deficiency of this vitamin leads to changes in cell structure and function which may become irreversible after a few weeks or months.

Of the minerals, calcium and iron are probably of greatest importance in the nutrition of older people (as of younger people). While it is a common belief that "milk is for babies, children, and pregnant women," osteoporosis is much too common in adults over 40 years of age. Although the role of calcium in osteoporosis is not clear,[24] Stieglitz[17] has pointed out that one factor may be poor utilization of calcium and phosphorus because gastric anacidity results in poor absorption of these minerals and of the fat-borne vitamins A and D. Whatever the cause of osteoporosis, the bulk of evidence favors 0.8 to 1.0 Gm. of dietary

calcium daily to promote optimum calcium nutrition in older adults.

Nutritional anemia is another condition frequently found in older persons. The anemia may result from deficiencies of iron, protein, B-vitamins (especially vitamin B_{12} and folic acid), vitamin C, or more likely to a combination of factors, again including reduced gastric hydrochloric acid. Fortunately, the best food sources of iron are also good sources of most of the other factors necessary for hemoglobin regeneration.

Water

Stieglitz,[17] Keys,[13] Thewlis,[11] and others have emphasized the importance of water in the diets of older persons. With diminished kidney function, water becomes increasingly important as a carrier, and eases rather than increases kidney burdens. "It is more work for kidneys to excrete a small amount of concentrated urine than a large amount of dilute fluid."[17] Drinking adequate amounts of fluids also helps in the control of constipation which so often plagues older people.

General Considerations

The bulk of evidence concerning good nutrition as a deterrent to the aging processes indicates that the best time to start practicing good food habits is before birth, or in one's youth at the latest. But much can be done if we "emphasize to young persons and those in the middle years that healthy aging is rarely fortuitous; that the earlier in life a start is made in achieving and maintaining optimum health, the more productive the effort will be."[31] Adults can change their food habits with results that sometimes surprise themselves. We frequently see diabetics who, with good instruction, not only keep their problem under control, but improve their general nutrition and zest for living. We have seen adults who attended nutrition classes during the war who still practice with enthusiasm the good nutrition they learned in time of stress. We have seen older adults with firmly fixed food habits who learned to eat (and enjoy!) vegetables and even liver, when the vegetables were properly prepared, colorful, and tastily seasoned, and the liver was mild-flavored and tender.

Often much can be done to keep the lives of older adults happy and productive, though it may sometimes take a little "mangling of food by ten thousand operations of cookery" to make the right foods sufficiently appetizing to be eaten with relish. But it is worth doing.

It takes three 8-ounce glasses of milk daily (not occasionally) to provide the 0.8 to 1.0 Gm. of calcium recommended for adults. Whole milk, buttermilk, or low fat milk are interchangeable in supplying this amount of calcium, but it would take about a quart and a half of ice cream to provide the same amount of calcium. Five or six ounces of orange juice will provide 75 mg. of ascorbic acid, but it would take five times that much pineapple juice to do it, and you just cannot do it with grape juice! It takes three glasses of milk, an egg, and four ounces of lean meat daily to provide 55 to 60 grams of protein. One just cannot be well nourished without taking thought. In expending ingenuity and imagination to make food attractive, let them be lavished on the basic, essential foods: milk, eggs, lean meat, fruits, vegetables, and whole grain or enriched cereals, and not squandered on fancy desserts and calorie-rich concoctions.

In the area of nutrition and aging, there is much that we do not yet know. But we already know a lot more than many of us practice.

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Food Poisoning

"Food poisoning, of course, has always been with us, but it has come into increasing prominence in recent years. . .

"The commonest type of food likely to be implicated is undoubtedly the 'made-up' meat dish, though the cream bun in the United States would seem to run it close. After all, we are prone to forget that meat and its products form the basis of most of the media on which we attempt to persuade organisms to grow in our laboratories, and milk and its derivatives equally provide an admirable environment for developing germs. The more a foodstuff is handled before consumption, the more likely it is to undergo infection. One practice in particular contributes greatly to the risk of poisoning—namely, the cooking of a food, allowing it to cool, and then reheating it. The fact that a dish is eaten hot gives us a false sense of security, although it may in fact contain a concentration of toxin that may be highly dangerous."

—Editorial. *The Medical Press* 230 (5): 117, 1953.

Nutrition Briefs

RECENT ADVANCES IN EXPERIMENTAL NUTRITION

VITAMIN B_6-deficient rats showed impaired ability to utilize ingested nitrogen.

J. R. Beaton, J. L. Beare, J. M. White, and E. W. McHenry. *J. Biol. Chem.* 200: 715, 1953.

IN PANTOTHENIC acid-deficient rats, adrenal hormone production was depressed and fat metabolism seriously deranged. Fat transport to the liver was prevented and could not be returned to normal by adrenocortical extract—perhaps because of concomitant changes in anterior pituitary hormone production.

A. F. Morgan and E. M. Lewis. *J. Biol. Chem.* 200: 839, 1953.

CABBAGE is dietetically more than a mere vehicle for ascorbic acid. Guinea pigs allowed an unlimited supply of cabbage grow more rapidly and have a lower incidence of infection than a corresponding group receiving synthetic ascorbic acid.

D. Brown, I. D. Ferguson, and A. G. Ramsay. *J. Physiol.* 121: 36, 1953.

POTASSIUM plays a critical role in amino acid utilization after protein depletion. Such depleted rats failed to respond when offered a complete source of amino acids if at the same time potassium was withheld.

D. V. Frost and H. R. Sandy. *Proc. Soc. Exper. Biol. & Med.* 83: 102, 1953.

ABSORPTION of oral cholesterol by rats was studied by analysis of the thoracic lymph and calculation of fecal cholesterol. Except for negligible amounts found in other organs or plasma, the absorbed cholesterol was found to be deposited in the liver. Cholesterol absorption in normal animals was increased by the administration of an excess of oral cholic acid.

M. Friedman, S. O. Byers, and E. Shibata. *J. Exper. Med.* 98: 107, 1953.

TUMOR-BEARING mice on a low calorie diet (7.4 cal.) survived 20 per cent longer, on an average, than tumor-bearing controls on a regular 13-calorie diet. Fewer additional mammary tumors and grossly visible lung metastases were noted in the animals on the low calorie diet.

A. Tannenbaum and H. Silverstone. *Cancer Res.* 13: 532, 1953.

ALLOXANIZED rats in diabetic coma have a marked increase in adrenocortical activity. Doca (desoxycorticosterone acetate) partially suppresses this activity and causes a fall in blood sugar.

S. Rose. *Australian J. Exper. Biol. & M. Sc.* 31: 273, 1953.

ANIMALS made hyperphagic by hypothalamic injury were found to have a significantly higher body temperature than either operated animals that were nonhyperphagic, or control animals. This was due neither to the nutritional state, to obesity, or to a breakdown of the body temperature-regulating mechanisms.

J. Mayer and R. M. Greenberg. *Am. J. Physiol.* 173: 523, 1953.

ANALYSIS of the free amino acids in serum, testes, and submaxillary glands of normal and vitamin A-deficient rats revealed no differences due to the lack of vitamin A.

M. Abdulnabi and J. G. Bieri. *Texas Rep. Biol. & Med.* 11: 181, 1953.

THE BIOSYNTHESIS of ascorbic acid is the result of a reaction between glucose and acetoacetate which appears to be enzymatic in nature.

M. C. Nath, and associates. *Proc. Soc. Exper. Biol. & Med.* 83: 39, 1953.

IN EXPERIMENTAL hypertension rutin was found to have no effect in altering the vascular lesions of hypersensitivity arteritis or in the prevention of arterial lesions under conditions described by the authors.

J. L. Orbison and E. Peters. *Proc. Soc. Exper. Biol. & Med.* 83: 173, 1953.

CURRENT OBSERVATIONS OF CLINICAL INTEREST

NUTRITIONAL macrocytic anemia is a deficiency of both folic acid and vitamin B_{12}, the deficiency of folic acid being the major and primary factor, while that of B_{12} is secondary in most cases.

Das Gupta, Chatterjea, and Basu. *Brit. M. J.* 2: 645, 1953.

ANALYSIS of amino acids in a number of specimens of serous fluids revealed the presence of certain amino acids. These included aspartic acid, glutamic acid, serine, methionine, and glycine, among others. Tyrosine was present in half the cases. No significant difference was found between those of malignant and nonmalignant etiology.

J. P. Ellis, W. W. Nowinski, and J. G. Bieri. *Texas Rep. Biol. & Med.* 11: 231, 1953.

Nutritional Quotes

Diet and Congenital Defects

"It is true that if a woman bears one malformed infant there is increased probability that subsequent children will also be malformed. This distribution would be expected from the facts of heredity, but it would also be expected from the facts of nutrition. Food habits are not easily changed, especially when there is no change in economic status. Furthermore, it is easy to suppose that a family may increase in size faster than does the income which supports it, and that the family diet becomes less adequate as the number of children increases. It is also easy to believe that if the protective foods become scarcer as the family becomes larger, a mother may deny herself in order to protect the child she has now and thus do irreparable damage to the child she will have in the future."

—A. G. Hogan. *Annual Review of Biochemistry* 22: 299, 1953.

Sodium Restriction and Sodium Deficiency

"There are . . . both drawbacks and complications to sodium restriction. As in any measure of this sort, the danger of an actual deficiency of the nutrient—in this case sodium—exists, and not only limits the use of the procedure but may result in disaster for the unwary. Recently, attention has been called to the occurrence of sodium deficiency in individuals on low-sodium diets. Not infrequently this acute deficiency is exaggerated or precipitated by other procedures, some of which are of at least quasi-nutritional nature, such as the excessive intake of fluids and the parenteral administration of glucose. Other procedures are pharmacologic, such as the use of mercurial diuretics. The deficiency of sodium may result in a depression of the output of urine, other changes in renal function, disturbances in electrolyte balance, azotemia, acidosis, and in some cases renal shutdown and death."

—J. B. Youmans. *Journal of the American Dietetic Association* 28: 1030, 1952.

Diet and Degenerative Heart Disease

"Our proclivity to develop early degenerative heart disease has been explained, on dubious grounds, by 'tension,' though what this is and how it is measured is not specified, by excessive obesity, and by physical indolence. Perhaps all of these play a role, but a strong argument can be made for the importance of the character of the diet. At least when different countries are compared there is a remarkable parallelism between the reported age-specific death rate from heart disease, especially coronary and myocardial disease, and the consumption of total fats in the diet."

Ancel Keys. *Geriatrics* 8: 620, 1953.

Diet, Cirrhosis, and Cancer

"The experimental work on hepatoma formation is of particular importance in view of the fact that in humans, cancer of the liver has a high incidence in populations subsisting on inadequate diets, as, for example, in Southern Africa and the Orient. It is an established fact that cirrhosis of the liver is a nutritional deficiency disease, and it is also true that where primary carcinoma of the liver occurs, cirrhosis is almost invariably present, suggesting that the malignant transformation has supervened in tissues already the seat of a severe nutritional deficiency disturbance. In the control of hepatic cancer, therefore, the need for preventive and curative measures against cirrhosis would seem self-evident."

—M. M. Suzman. *South African Medical Journal* 23: 401, 1949.

Eskimo Diet

"The Eskimos used to subsist on a carnivorous diet, eating meat raw or lightly cooked with sea water, and consuming heads, skin, viscera, marrow, blood, and stomach contents. This was an excellent dietary adequate in all respects and only failing when the hunting of seals or other animals was prevented. Despite almost complete lack of hygiene they enjoyed a healthy, happy life. The Bush Indians fared similarly upon cooked meat with some berries and nuts. The introduction of the white man's diet in return for his exploitation of the furs and extermination of the buffalo changed matters. The Indian has so far been most affected, but wherever the white man contaminates the Eskimos, the diseases of civilization follow."

—H. M. Sinclair. *Proceedings of the Nutrition Society* 12: 79, 1953.

Aboriginal Australian Etiquette

"Elaborate customs decide about what part of a carcass goes to whom and vary with the tribe. If a number of people catch an animal there is an official cutter-up who helps himself to the kidneys and the heart. If a kangaroo, however, is killed by an unmarried man assisted by a married man, everything goes to the wife's parents except the left hind-leg, which goes to the brother and the right hind-leg which goes to the unmarried man. Some animals are shared between everybody. If a married man catches an emu, he eats the intestines, liver, and gizzard, the legs go to his wife's father, and the body is shared by his own parents."

—G. H. Bourne. *Proceedings of the Nutrition Society* 12: 60, 1953.

Reviews of Recent Books

Biochemistry and Physiology of Nutrition, Vol. I, by G. H. Bourne and G. W. Kidder, Academic Press, New York, 1953, pp. 471, $13.00.

This work is one of the most significant to appear in the nutritional field in recent years. It (Volume I of a two-volume set) consists of a group of monographs, written by recognized authorities, which summarize the important work to date.

The scope may be appreciated from a partial list of the chapter titles: Water and Electrolyte Metabolism, Vitamins and Hematopoiesis, Carbohydrate Metabolism, The Biosynthesis of Proteins, etc.

This is a joint Anglo-American work. Not only do the two editors span the Atlantic, but six of the eleven chapters were written by English scientists. The reviewer thinks this is an excellent idea since there is no place in science, especially in a "global" science like nutrition, for nationalistic in-breeding.

The title—*Biochemistry and Physiology*—is appropriate since the work deals primarily with investigations of a basic science nature; in fact, as the preface states, the book "is directed to all workers dealing with problems of metabolism as well as to the nutritionist, for the science of nutrition has come to encompass metabolic reactions as well as new materials."

An excellent author and subject index makes the plethora of information readily available. Thus the book serves admirably as a current reference and source book for the serious nutritionist.

Although this treatise does not touch on human or clinical nutrition to any great extent, nor was it presumably the intent to do so, one would expect a more detailed account, for example, of pantothenic acid and its relation to coenzyme A—certainly a matter of fundamental biochemical-nutritional importance.

Furthermore (and one can always pick a flaw), although there are three references plus one table on the ascorbic acid content of semen, there are only brief paragraphs on obesity and rickets. There is also a certain curious imbalance in chapter length, so that while vitamin C is covered exhaustively in 101 pages and 765 references, all the fat-soluble vitamins are considered in twenty-five pages and 104 references. Nevertheless, the material, as presented, is lucid and important; and we are grateful for the large amount of work that obviously went into this text.

The volume can be highly recommended to all workers in the broad fields of human and animal nutrition. S.O.W.

Familial Nonreaginic Food-Allergy (third edition) by Arthur F. Coca, M.D., Charles C Thomas, Springfield, Ill., 1953, pp. 279, $10.50.

Arthur F. Coca, one of the American pioneers in the investigation of allergic diseases and the originator of the term "atopy," has studied the problems of food allergy for many years. Prominent among the difficulties in this field are the failure to demonstrate allergic antibodies ("reagins") and the absence of cutaneous sensitivity to the incriminated foods in affected persons. In this third edition of his book on the subject, Coca has described his most recent findings and techniques after eight more years of investigation, and has incorporated reports by a few other workers. From his researches has evolved the idea of familial nonreaginic food-allergy, designated as the fifth category of allergic disease along with atopy, allergy of infection, serum-disease, and contact dermatitis. The same concept, expanded to embrace other excitants such as tobacco smoke, house dust, and drugs, has more recently been termed "idioblapsis."

This form of allergy is thought to be identifiable by the pulse-accelerating effect in susceptible individuals of the ingestion of the causative food or exposure to other allergens. Other important characteristics of idioblapsis include a hereditary influence independent of atopic inheritance, a symptomatology not represented in the atopic group, and a specificity unrelated to humoral antibodies but intimately and mysteriously tied in with the sympathetic nervous system. Idioblapsis is considered to be a familial, constitutional disease, the protean manifestations of which reflect the differing localization of the "shock-tissue." No organ can be assumed to be exempt. Recognized by Coca as idioblaptic symptoms are headache, tiredness, indigestion, constipation, heartburn, nervousness, dizziness, neuralgia, canker-sores, eczema, irritability, depression, conjunctivitis, angina pectoris, and others. The primary gross pathologic lesions of idioblapsis thus far recognized consist of edema caused by obstruction of efferent lymph channels and of ulcer. It is claimed that 80 to 90 per cent of the population are affected with idioblaptic allergy.

The recognition and management of familial nonreaginic food-allergy has been simplified by the newer plan of pulse-testing single foods at one or one and one-half hour intervals throughout the day. The difficulties and "art" of interpreting the pulse-diet record are thoroughly discussed. In cases otherwise

uncontrollable or even undiagnosable, sympathetic ganglionectomy or stellate ganglion block has been performed. Numerous case reports illustrate all phases of the subject.

Although Coca has provided a provocative approach to an important problem in the realm of allergy and despite the scholarliness of the presentation, it has not been widely accepted by either practical or theoretical workers in the field—a skepticism frankly acknowledged in one of the Prefaces. It is admitted by Coca that the fully developed pulse-dietary procedure cannot well be fitted into the program of the practicing physician but would require the establishment of specially manned diagnostic centers. Certainly, the part played by idioblapsis in predisposing to such conditions as essential hypertension, angina pectoris, the common cold, low-grade infections, cancer of the breast, epilepsy, multiple sclerosis, poliomyelitis, peptic ulcer, hemorrhoids, dysmenorrhea, disturbances of the climacteric, glaucoma, diabetes mellitus, and other diseases, must receive far greater scientific confirmation before general acceptance can be expected. The deficiencies of skin testing techniques in identifying food allergies have long been recognized. Whether pulse-diet methods constitute a solution of the problem remains to be proved.

In summary, Coca's book deserves careful reading by advanced students of allergy who may be persuaded to attempt large-scale verification of his claims, but can scarcely be recommended to others.

P. M. GOTTLIEB

Water, Electrolyte and Acid-Base Balance. Normal and pathologic physiology as a basis for therapy by Harry F. Weisberg, M.D., Williams & Wilkins Company, Baltimore, 1953, pp. 232, $5.00.

Since "water and electrolyte metabolism is an integral part of every branch of medicine and biology," it is a subject of tremendous importance in clinical practice. Recently, a number of books have been published which aim to act as guides through the complex maze of clinical chemistry. This new monograph, in many ways, is the best of the lot. With 29 tables, ten figures, and 398 references, it quite completely covers the subjects of body water, electrolytes, acid-base regulation in normal and abnormal situations. The reader will find the last ninety pages particularly useful in that theoretical considerations are applied to practical bedside problems. Intended to be a source book, the book does fulfill this objective admirably.

Two minor criticisms may be made. There is a tendency to document many statements which this reviewer believes do not require substantiation. For example, one need not give a reference for "Edema is a term applied to swellings produced by an excess accumulation of the extracellular fluid." In addition, the subject matter does not lend itself to a flow of words and, in some sections, the short factual statements make for slow reading.

These, however, are minor matters. In this book a wealth of material, often not familiar to the practicing physician, is readily available. The tables and charts are particularly helpful, and the physiologic and biochemical background is sound. Very few, if any, matters of importance appear to have been omitted.

With the help of the adequate index, every reader will find this manual a useful and reliable aid in the diagnosis and treatment of fluid and electrolyte problems. It can be strongly recommended. S.O.W.

Holt Pediatrics (twelfth edition) by L. Emmett Holt, Jr., and Rustin McIntosh, Appleton-Century-Crofts. Inc., New York, 1953, pp. 1485, $15.00.

Those pediatricians who had used "Holt & McIntosh" as their school textbook of pediatrics, and awaited the appearance of the new volume with interest, were not disappointed.

The twelfth edition follows the previous editions in that a continuity of style is maintained by rigid editing of the two senior authors. The book is flowingly readable and the information is concise.

Certain chapters are especially worthy of note. The section on the newborn is practical and informative. The nutritional section has an easily understandable portion on the physiology of nutrition, as well as the essentials of growth and development.

The system review is sometimes sketchy. but all the basic diseases are at least mentioned. The handling of the retarded child is interesting and detailed. The section on poisoning appears too short to be of value.

I believe that this book will be equally valuable to the medical student, the hospital resident, the general practitioner, and the practicing pediatrician. It is not suitable, in spite of an extensive bibliography, to anyone attempting to use this as a source book of advances in pediatrics. P.G.

Books received for review by the *Journal of Clinical Nutrition* are acknowledged in this column. As far as practicable those of special interest are selected, as space permits, for a more extensive review.

Vitamin Manual, Upjohn, Kalamazoo, 1953, pp. 90.

Review of Physiological Chemistry (fourth edition) by H. A. Harper, Lange Medical Publications, Los Altos, Calif., 1953, pp. 329, $4.00.

Biochemistry and Physiology of Nutrition. Vol. II, edited by G. H. Bourne and G. W. Kidder, Academic Press Inc., New York, 1953, pp. 641, $15.00.

Abstracts of Current Literature

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GERIATRIC NUTRITION

The establishment of dietary requirements for aged persons is a subject of much current interest. In association with the aging process, there is a reduction in the basal metabolic rate, which may be reflected in a lower requirement for calories and for the biocatalysts essential in body metabolism. The frequency with which nutritional deficiency is encountered in the elderly is more likely due to improper dietary habits rather than to increased requirements for nutrients. An excellent survey of this problem is found in the following papers.

Dietary Requirements of the Aged. M. K. Horwitt. *J. Am. Dietet. A.* 29: 443, 1953.

The problem in geriatric nutrition (as at other ages) is to find how to induce the older individual to choose and to like what is good for him. Controlled research at Elgin State Hospital has not produced evidence that the basic nutritional requirements of the healthy older man are essentially different from those of younger individuals. There is little doubt that more signs of nutritional inadequacy may be found in older men than in younger individuals, but there is no reliable evidence to indicate that these differences are due to increased requirement for nutrients.

Comparative glucose tolerance curves for 19 older men (average age 70 years) and 13 men of average age 30 years indicated no impairment of glucose absorption from the gastrointestinal tract. Blood pyruvic acid in the same men after intravenous or oral administration of glucose showed pyruvate values lagging behind the glucose values in older men after intravenous administration, suggesting a metabolic deficiency not present in the younger men.

The older person can absorb nutrients and retain them as efficiently as the young person. This was illustrated by studies of thiamine and riboflavin depletion and repletion. Six older men (71, 62, 66, 78, 65, and 81 years of age) and five young men (44, 30, 36, 28, and 30 years of age) were fed a diet containing 4 mg. thiamine and 3.1 mg. riboflavin daily for two years. Following this control period, the men were restricted to 0.2 mg. thiamine and 0.75 mg. riboflavin. A sharp drop in urinary thiamine ensued and reached a minimum of 0.01 mg. after three months. Data for older and younger men overlapped. Urinary riboflavin dropped from 1 mg. to 0.08. Again, data for both age groups were similar. Current studies on niacin and protein requirements do not indicate a difference for the young and old. Both maintained positive nitrogen balance during six months on diets supplying 6.5 Gm. nitrogen per day.

The authors have demonstrated that when vitamin deficiencies occur there are definite biochemical and clinical differences between young and old. Levels of blood lactic and pyruvic acid rise to higher levels during thiamine deficiency in old men. Anorexia appeared earlier in the older men, though edema and loss of tendon reflexes did not seem to appear any sooner in the old. Return of lost Achilles tendon reflex was particularly slow in the old men; in one case it did not return until after 18 months of supplementation.

The lower basal metabolic rate of the healthy old man is evidence that he needs fewer calories—assuming that his protein needs are of the same order as

when he was younger, and the protein content of the diet should be increased. At the Elgin State Hospital it was ascertained that bread was a preferred food of many of the aged, so a high protein bread supplying 44 Gm. protein per pound of bread has been devised. The bread is supplemented with dried eggs as well as milk powder. More chopped foods are served to older patients. Foods such as rhubarb, cabbage, corn, and cucumbers are limited, and milk consumption is encouraged. The use of low fat dairy products is being increased to improve the protein:fat ratio.

Horwitt emphasizes that the problem in feeding the older generation is not one of requirements. Rather, it is one of logistics: how to package and move some of our food supply to those individuals who are not consuming enough of the right kind of metabolic ammunition.—J. SMITH

Utilization of an Improved Diet by Older Women. M. A. Ohlson, L. Jackson, R. M. Beegle, D. Dunsing, and E. C. Brown. *J. Am. Dietet. A.* 28: 1139, 1952.

Eighteen women 48–77 years of age were chosen for study because each one seemed able to maintain an unusual amount of productive activity for her age, and because physical examination revealed no specific symptoms of food deficiency. Each woman recorded the weight of food eaten for 3–4 consecutive months. Six 5-day balance periods were completed for 16 of the women. Diets were self-selected from food of the woman's choice. Two periods were studied to represent the customary diet and the milk intake was adjusted so that it supplied approximately 250, 500, or 700 ml./day (each level for two of the six balance periods). Two weeks were allowed between the balance periods in which milk was adjusted. Mean data for nitrogen, calcium, and phosphorus retentions and intakes and caloric intakes for each of the six experimental periods are presented.

When nitrogen, phosphorus, and calcium intakes and retentions were plotted against increasing calorie intakes, it was shown that losses of nitrogen and phosphorus occurred in the majority of subjects at all calorie intakes of less than 1800 per day. The data on calcium equilibrium were considered more difficult to interpret because of the range of intakes. The reviewer believes that all of the calorie comparisons would have been more significant if the intake of the other nutrients had remained constant.

The authors make no definite conclusions in the paper. They suggest that 1.0 Gm. calcium per day for the adult is necessary if the dietary allowances are to meet the needs of 90 per cent or more of the adult population. They recommend a wider use of milk by aging adults because of its nutritive value and relative low caloric contribution, and express the belief that many aging women would gain increased vitality if counseling included a careful evaluation of food habits.—J. SMITH

Elderly patients sometimes develop a dislike for protein foods, which may result in difficulties in maintaining nitrogen equilibrium. Because of difficulties encountered in protein feeding, various hormones were examined to ascertain their effect upon protein metabolism. It is of interest that insulin was found effective in producing a positive nitrogen balance in such patients.

The Influence of Some Hormonal Substances on the Nitrogen Balance and Clinical State of Elderly Patients. W. B. Kountz, P. G. Ackerman, and T. Kheim. *J. Clin. Endocrinol.* 13: 534, 1953.

The authors have previously shown that elderly individuals require more protein to maintain nitrogen balance than do young adults, their balance is more easily disturbed by stress, and they require a longer time interval to re-establish nitrogen equilibrium. The administration of androgens generally increases the retention of ingested protein. This is of particular importance because of the difficulties encountered in attempts to augment the protein intake of elderly subjects. The present report deals with an investigation of the effects of other agents. Thyroid extract, Terramycin®, aluminum silicate, and a placebo produced no significant changes in protein metabolism. Protamine zinc insulin, in doses of 50 to 100 units per day, produced a slight but definite positive balance. Cortisone (100 mg. per day) and ACTH (15 to 60 mg. per day) induced nitrogen excretion with a return to positive balance during continued administration. The results of this study indicate that protamine zinc insulin may prove of value, and it is hoped that the authors will pursue this aspect of the study further.—N. G. SCHNEEBERG

It is demonstrated that the higher levels of protein intake in older people may actually induce anorexia, so that the total intake of food may actually be decreased on high protein diets.

Effects of Increased Protein Intake in Older People. W. B. Kountz, P. G. Ackermann, T. Kheim, and G. Toro. *Geriatrics* 8: 53, 1953.

In order to determine the amount of protein that could be tolerated in a diet, particularly when the source was meat, eggs, and milk, 4 elderly subjects were studied by the nitrogen-balance technique. The daily intake of protein was increased from 1 Gm./Kg. of body weight per day to 1.5 Gm./Kg. for 75 days. This was supplemented with a chopped meat product. Three patients received 2 Gm. of protein and one later received 2.5 Gm. These diets all furnished approximately the same number of calories. With increased protein intake, patients complained of satiation and it was more and more difficult to maintain the desired intake. The satiation point varied from 1.5 to 2.5 Gm. of protein per Kg. in individual patients, and the total amount from 100 to 125 Gm. per day. It is important to note that, on the highest diet offered a patient, the actual protein intake, because of an induced anorexia, was often lower than when he ate all the food on a lower protein diet. The

author concludes that difficulties may be encountered in maintaining elderly persons on high protein diets over long periods of time when the intake is more than 1.5 Gm./Kg.—S. O. WAIFE

The specific dynamic action of protein in older men, although delayed in its peak effect, is not significantly different from that of younger individuals. Like other physiologic effects, it is slower in the aged.

Specific Dynamic Action of Protein in Men Past 60 Years of Age. W. W. Tuttle, S. M. Horvath, L. F. Presson, and K. Daum. *J. Applied Physiology* 5: 628, 1953.

The responses to a standard protein test meal which yielded 25 Gm. were studied. Specific dynamic action was expressed as total excess oxygen utilization. Two groups were compared: young men of a mean age of 24 years, and old men having a mean age of 77 years. In the older age group, the onset of the response to the protein meal was slower. However, this group had higher peak values and had an increase in excess oxygen consumption during the latter half of the 4.5-hour test period.—M. J. OPPENHEIMER

VITAMIN B_{12}

The oral administration of vitamin B_{12} is ineffective unless intrinsic factor is present. The action of intrinsic factor in promoting the absorption of this vitamin is not clearly understood at the present time. However, the isolation of protein factors from stomach concentrates makes it possible to treat by the oral route patients in whom the intrinsic factor is lacking. Certain of the characteristics of the intrinsic factor-vitamin B_{12} interrelationship are discussed in the following paper.

Concentration of Intrinsic Factor and Vitamin B_{12} Binding Activities of Fraction of Desiccated Hog Stomach. W. H. Prusoff, A. D. Welch, R. W. Heinle, and G. C. Meacham. *Blood* 8: 491, 1953.

Preparations with concentrated intrinsic factor activity were prepared from Ventriculin® by 2 per cent sodium chloride extraction, filtration, pH adjustment, ammonium sulfate precipitation, and dialysis until all ammonium had disappeared. Three fractions were obtained and were tested for intrinsic factor activity in patients with pernicious anemia in relapse and for B_{12}-binding potency as measured by their capacity to prevent the growth of *Lactobacillus leichmanii* in the presence of vitamin B_{12} and by a dialysis method.

By these procedures the intrinsic factor activity was concentrated in an amount of protein equivalent to 0.03 per cent of the original weight of crude material. The protein was not homogeneous, however. Fractions with the highest intrinsic factor in patients with pernicious anemia in relapse bound the least amount of vitamin B_{12}. This work not only increases our knowledge about the purification and concentration of the intrinsic factor, but adds additional evidence that vitamin B_{12}-binding and intrinsic factor activity are separate functions. Others have reported similar results, and have shown that the heat lability of intrinsic factor activity is not shared by vitamin B_{12}-binding capacity.—R. W. VILTER

Experience with one of several commercial preparations containing the intrinsic factor-vitamin B_{12} combination has demonstrated that the oral therapy of pernicious anemia is satisfactory.

Antianemic Properties of Reaction Products of Vitamin B_{12} and the Intrinsic Factor. T. D. Spies, R. E. Stone, R. M. Suarez, G. Garcia-Lopez, R. Lopez-Toca, and A. Reboredo. *J. A. M. A.* 151: 1264, 1953.

These authors studied the effects of vitamin B_{12} and a concentrated intrinsic factor preparation in 11 patients: 8 with pernicious anemia, 1 with nutritional macrocytic anemia, and 2 with tropical sprue. During an adequate control period on a meat-free diet, these subjects did not respond to 10 to 15 μg. of crystalline vitamin B_{12} orally, but they did respond when they received a commercial preparation containing the intrinsic factor as well as vitamin B_{12}.

From these and other studies, the authors conclude that the average patient with pernicious anemia responds better than the average patient with tropical sprue to the administration of vitamin B_{12} and intrinsic factor concentrate; and they also show that oral therapy of pernicious anemia is possible in selected cases.—S. O. WAIFE

Megaloblastic anemia resulting from a massive resection of the small intestine was demonstrated to respond to treatment with vitamin B_{12}.

Massive Resection of the Small Intestine: A Six Year Follow-Up Study. J. K. Berman and E. D. Habegger. *Am. J. Dig. Dis.* 20: 152, 1953.

A six-year follow-up study is presented of a patient who had been subjected to resection of all the jejunum except for 45 centimeters, the ileum, and the ascending colon. A macrocytic anemia developed very slowly, associated with weakness, atrophic glossitis, atrophic proctitis, and paresthesia of the hands and feet. Liver function studies were normal. Gastric analysis with histamine stimulation revealed the presence of free acid. Sternal biopsy revealed megaloblastic marrow. Institution of vitamin B_{12} therapy resulted in clearance of the anemia and associated symptoms. The diarrhea, which had been most troublesome, also responded to vitamin B_{12} therapy, but the patient has found it necessary to remain on a fat-free diet.—S. H. LORBER

Experimental "evidence" that vitamin B_{12} has a direct effect upon renal function and electrolyte metabolism is not borne out by the following clinical study.

On the Presumed Diuretic Action of Vitamin B_{12}. G. D'Antuono. *Acta Vitaminol.* 6: 199, 1952.

Vitamin B_{12} was tested for diuretic action in 3 healthy subjects and 4 with heart disease of various etiologies. All received the same diet, containing 8.1 Gm. of salt, and liquids were limited to 1000–1500 cc. per day. After several days of this regimen, blood, K, Na, and Cl, and 24-hour urine chlorides were determined; a 5-day period of treatment with 30 μg. of vitamin B_{12} per day was then begun, during which time daily determinations of the same constituents were made.

No noteworthy changes in the blood constituents examined occurred in the 3 healthy subjects. In the cardiac patients, the variations in the same constituents were slight and irregular, and collateral control tests in cardiac patients receiving no vitamin B_{12} showed similar daily variations. The author concludes that vitamin B_{12} does not appear to produce any direct interference in electrolyte metabolism, either in normal subjects or in patients with heart disease.

In 2 of the 3 healthy subjects, the urine volume was unaffected by administration of vitamin B_{12}; in the third case, an initial rise with subsequent return to normal is attributed by the author to a probable consumption by the subject of a larger amount of liquids than that allowed. In the cardiac patients, urine excretion remained almost constant, except for alterations corresponding to changes in the state of decompensation.

The author concludes that vitamin B_{12} has no specific diuretic action and is incapable of modifying water or salt retention or elimination either in normal individuals or in subjects with cardiocirculatory decompensation. Therefore the hypothesis that vitamin B_{12} is directly related to renal function must be considered doubtful.—C.-J. Howell

Since cobalt is present in vitamin B_{12}, it would seem to be an essential trace element in the endogenous formation of vitamin B_{12}. The administration of cobalt in conjunction with vitamin B_{12}-deficient diets is capable of stimulating growth in certain species. In addition, there is a report of some studies on cobalt metabolism in humans.

Effect of Cobalt in Diet of the Chick. R. L. Davis, G. M. Briggs, and H. J. Sloan. *Proc. Soc. Exper. Biol. & Med.* 82: 175, 1953.

Chick growth was stimulated by the addition of 10–100 mg. of cobalt sulfate per Kg. of corn-soybean oil meal in B_{12}-deficient diets. No effect was produced when cobalt sulfate was added to diets containing adequate amounts of B_{12}.—L. W. Kinsell

Cobalt Metabolism of Young College Women on Self-selected Diets. M. J. Harp and F. I. Scoular. *J. Nutrition* 47: 67, 1952.

The interest in cobalt metabolism has been stimulated by the finding that it is part of the vitamin B_{12} molecule. This study was undertaken to determine the cobalt metabolism of young college women consuming self-selected diets. Twenty-three young college women served as subjects while living in the Home Management House, North Texas State College. The study was carried out during four 5-day metabolism periods. Each group of women purchased and prepared its food separately. A serving of each food from each meal, similar in all respects to that eaten by the college women, was collected in weighed, aged glass jars at the same time that the subjects were served at the table and analyzed for cobalt. Milk was analyzed separately. There were minute traces of cobalt in the drinking water; therefore, it was considered negligible in the total daily intake.

The positive retentions ranged from 0.02 to 5.64 μg. per day on total daily intakes of 5.63 to 7.79 μg. of cobalt. The main pathway of excretion was through the urine, with an average of 67 per cent of the total daily intake appearing in the urine.—B. Sure

Vitamin B_{12} deficiency in animals and pernicious anemia in humans are associated with a marked reduction of the sulfhydryl content of the blood. Anemias associated with iron or folic acid deficiencies do not manifest this alteration. Thus the determination of blood sulfhydryl levels may represent a differentiating point in the diagnosis of anemia. The administration of vitamin B_{12} will promptly increase the sulfhydryl levels.

The Effect of Vitamin B_{12} on the Levels of Soluble Sulfhydryl Compounds in Blood. C. T. Ling and B. F. Chow. *J. Biol. Chem.* 202: 445, 1953.

This report is the result of a study of the levels of soluble sulfhydryl compounds in the blood of vitamin B_{12}-deficient rats and their vitamin B_{12}-injected and normal controls, and of the blood sulfhydryl content of patients with pernicious anemia in relapse, before and after B_{12} treatment. The data reported indicate that vitamin B_{12} deficiency in rats caused a marked diminution of soluble sulfhydryl compounds in blood cells. A similar abnormality was observed in patients with pernicious anemia in relapse. Administration of vitamin B_{12} to either deficient rats or patients with pernicious anemia was followed by a significant rise in the levels of soluble sulfhydryl compounds in the blood which eventually became stabilized at a level comparable to those of healthy individuals. The authors point out that in folic acid hypovitaminoses, or anemia due to iron deficiency, the soluble sulfhydryl levels in the blood are essentially unaltered and that these facts may be useful in the clinical diagnoses of megaloblastic macrocytic anemias in differentiating between vitamin B_{12} and folic acid deficiencies. The changes in blood sulfhydryl levels

were primarily due to those of a concentration of glutathione. Ergothionine levels in the blood also showed some fluctuation prior to and following vitamin B_{12} therapy.—M. K. HORWITT

The influence of vitamin B_{12} upon the activity of specific enzyme systems of the liver has been investigated with particular reference to the effect of the action of an antivitamin B_{12} preparation.

Effect of a Vitamin B_{12} Deficiency on Liver Enzymes in the Rat. J. N. Williams, Jr., W. J. Monson, A. Sreenivasan, L. S. Dietrich, A. E. Harper, and C. A. Elvehjem. *J. Biol. Chem.* 202: 151, 1953.

The liver enzymes, transmethylase, xanthine oxidase, endogenous respiration, and choline oxidase were investigated for the possible involvement of vitamin B_{12} in specific enzyme systems. The growth of male rats of the Sprague-Dawley strain was investigated on four different regimes. Group I served as the negative control and received only the basal ration. Group II animals were injected with an "antivitamin B_{12}" preparation which has been reported to be a specific antagonist to vitamin B_{12} for *Lactobacillus leichmannii*. Group III rats received an intraperitoneal injection of 2 μg. of crystalline vitamin B_{12} in solution each day. Group IV was given both the "B_{12} inhibitor" and—a few minutes later—the B_{12} as in Group III. The average weights of the rats after 5 weeks on these diets were: Group I, 176 Gm., Group II, 177 Gm., Group III, 238 Gm., and Group IV, 241 Gm., respectively, indicating that the vitamin B_{12} antagonist had no apparent effect on the growth of the rats in this experiment. Analyses of the livers of these animals at the end of the experimental period indicated that there was a decrease in liver and endogenous respiration in simple vitamin B_{12} deficiency. This was accompanied by a decrease in the activity of betaine-hemocystine transmethylase and xanthine oxidase. Liver choline oxidase activity seemed to be increased by the vitamin deficiency.—M. K. HORWITT

Effect of Vitamin B_{12} Deficiency on Chick Plasma Proteins. J. M. Hsu, J. R. Stern, and J. McGinnis. *Arch. Biochem. & Biophys.* 42: 54, 1953.

When White Leghorn chicks were fed a vitamin B_{12}-deficient diet there was a relative decrease in the level of total plasma protein in the deficient chicks as compared with protein levels in chicks supplemented with 30 μg. of crystalline vitamin B_{12}/Kg. diet. Fractionation of the plasma proteins by means of sodium sulfate (Howe's method) indicated that the vitamin B_{12}-deficient chicks had less euglobulin, less pseudoglobulin II, and less total albumin than the supplemented group. Prothrombin times were higher and fibrinogen levels were lower in the deficient chicks than in the supplemented chicks. The possibility that vitamin B_{12} function is related to the genesis of ribonucleoprotein is discussed briefly.—M. K. HORWITT

VITAMIN E

Vitamin E has been demonstrated to be of importance in the experimental animal. It has an influence upon the reproductive activity, upon muscle and nervous tissue, and upon the liver as demonstrated by its ability to prevent hepatic necrosis under certain conditions. However, the importance of vitamin E in human nutrition has not been well established. Investigation as to its possible importance in human and experimental nutrition continues.

The Etiology of Nutritional Muscular Dystrophy. I. R. Telford. *Texas Rep. Biol. & Med.* 11: 366, 1953.

Previous studies have shown that deficiency of vitamin E (alpha-tocopherol) led to a form of muscular dystrophy which may have had circulatory disturbances as the underlying mechanism. In this investigation, dystrophic vitamin E-deficient rabbits had alterations of the blood supply to the thigh muscles produced by unilateral sympathectomy, sciatic nerve resections, or femoral artery ligation. In these animals, no significant difference in the histologic picture of the operated and unoperated thigh muscles was noted. The author concludes that it is unlikely that variations in blood supply to the striate muscle are etiologic factors in the production of the muscular lesions observed in nutritional muscular dystrophy following vitamin E deficiency in rabbits.—S. O. WAIFE

Availability of Vitamin E in the Newborn Infant. P. György, G. Cogan, and C. S. Rose. *Proc. Soc. Exper. Biol. & Med.* 81: 536, 1952.

Erythrocytes of rats deficient in vitamin E may be hemolyzed by dialuric acid *in vivo* and *in vitro*, and also by a dilute solution of hydrogen peroxide. Vitamin E, given *in vivo* or added to suspensions of red cells *in vitro*, prevents the hemolysis by dialuric acid as well as by hydrogen peroxide. Red blood cells in newborn infants are hemolyzed by dilute solutions of hydrogen peroxide. This hemolysis may be prevented by vitamin E *in vitro* or *in vivo*. However, even with five daily doses of vitamin E, given the mother during the last weeks of pregnancy, the hemolysis test in the newborn remained unaltered. The authors believe that the difference between rats and humans is because of less easy passage of vitamin E through the placental barrier in the human.—L. W. KINSELL

An Elevated Xanthine Oxidase in Livers of Vitamin E-Deficient Rabbits. J. S. Dinning. *J. Biol. Chem.* 202: 213, 1953.

Previous publications of the author had indicated a relationship between vitamin E and nucleic acid metabolism. He had shown that deficient rabbits exhibited increased amounts of allantoin. The present study investigated the influence of vitamin E

deficiency on the xanthine oxidase activity of rabbit liver homogenates. White New Zealand rabbits weighing 600 Gm. were given a purified vitamin E-deficient diet and controls were given the same diet plus oral doses of 4 mg. of alpha-tocopherol acetate on alternate days. Other controls were fed commercial rabbit chow. When the animals on the deficient diet exhibited signs of muscular dystrophy, creatinuria, and elevated allantoin excretion, they were sacrificed along with the controls, and xanthine oxidase and the uricase activity was determined on liver homogenates from these animals. Whereas the liver homogenates from normal rabbits were devoid of xanthine oxidase activity, liver homogenates from vitamin E-deficient rabbits contained high levels of xanthine oxidase. Neither alpha-tocopherol phosphate nor methylene blue decreased the *in vitro* xanthine oxidase activity of the homogenates.—M. K. Horwitt

Both vitamin E and the adrenal cortical hormones have been employed in the treatment of certain collagen diseases. The following work indicates that vitamin E has no influence on the pituitary-adrenal axis.

On the Relationship between Vitamin E, Anterior Pituitary and Adrenal Cortex. B. Bonati, R. Lorenzini, and G. C. Manfredi. *Acta Vitaminol.* 6: 193, 1952.

The plethora of contradictory clinical and experimental data on the action of vitamin E, and the various hypotheses advanced to explain them, led the authors to investigate the relationships between vitamin E and the pituitary-adrenal axis, as reflected in the urinary excretion of 17-ketosteroids and in variations in circulating eosinophils. Confusing evidence on the relations between corticotropic hormone, cortisone, and cholesterol, and on the relation of vitamin E and cholesterol, suggested the study of the behavior of cholesterol in nonatherosclerotic subjects receiving vitamin E.

Twenty-eight healthy subjects, aged 20–45 years, divided equally as to sex, were studied. One group, whose average daily elimination of 17-ketosteroids and blood cholesterol level had been previously determined, was given intramuscular α-tocopherol acetate (300 mg. per day) for 6 consecutive days, after which the urinary constants and blood chemistry determinations were repeated. A second group, fasted from the previous evening, received 600 mg. of vitamin E by the intramuscular route, after prior determination of the circulating eosinophils, and 6 hours later the eventual granulocyte variations were evaluated.

The results were substantially negative. Continuous administration of vitamin E did not appreciably modify the urinary elimination of 17-ketosteroids in individuals of either sex. Nor were there, in the same subjects, significant changes in blood cholesterol level, or any correspondence between variations in 17-ketosteroid excretion and in the lipids examined.

In the second group of subjects there were no significant variations in circulating eosinophils after administration of 600 mg. of α-tocopherol acetate.

It would seem on the basis of these results that vitamin E does not directly stimulate adrenal endocrine function or excite pituitary corticotropic activity. The simultaneous absence of variations in urinary 17-ketosteroids, blood cholesterol, and circulating eosinophils would suggest as much.

Their negative conclusions as to the stimulating action of vitamin E on the pituitary-adrenal axis led the authors to doubt the efficacy of the vitamin in the large and heterogenous group of diseases which are benefited by treatment with pituitary and adrenal hormones.—C.-J. Howell

LIPID METABOLISM

The formation of fat is currently believed to depend upon the presence of carbohydrate precursors which in the presence of insulin are reduced to the acetate level, from whence they are incorporated into fatty acid molecules. Using an amorphous preparation of insulin, containing the hyperglycemic glycogenolytic factor (glucagon), a decrease in fatty acid synthesis was observed, while the crystalline preparation had a stimulatory effect upon lipogenesis.

The Effect of Hyperglycemic-Glycogenolytic Factor and Epinephrine on Fatty Acid Synthesis. E. S. Haugaard and W. C. Stadie. *J. Biol. Chem.* 200: 753, 1953.

This investigation is concerned with the effects of insulin, hyperglycemic factor, and epinephrine on the incorporation of radioactive acetate into fatty acids by rat liver slices. A decrease in fatty acid synthesis was observed with an amorphous preparation of insulin, but the stimulatory effect of insulin on the incorporation of acetate into liver fatty acids was confirmed when a crystalline preparation was used. This effect was thought probably due to the presence of hyperglycemic factor in the amorphous preparation.

Assays determining the effects of these hormonal preparations on glycogenolysis showed acceleration by amorphous insulin, hyperglycemic factor, and epinephrine, but no effect by crystalline insulin.

It is possible that the effects of these hormones on the incorporation of acetate into fatty acids may be related to the increase in glycogenolysis, with a resulting extra formation of pyruvate. This pyruvate may be converted into a two-carbon fragment which dilutes the pool of radioactive acetate and decreases the specific activity of the fatty acids.—M. K. Horwitt

Since the sorbitan derivatives have been used to promote fat absorption, it is of interest to observe

that these substances have an inhibitory effect upon pancreatic lipase. The use of these emulsifying agents in man is noted, but other reports stress the numerous factors influencing the absorption of fat.

The Inhibition of the Action of Pancreatic Lipase by Esters of Polyoxyethylene Sorbitan. F. N. Minard. *J. Biol. Chem.* 200: 657, 1953.

In recent years the "Tweens" have been used to promote intestinal fat absorption and to assist in the formation of fat emulsions for clinical use. It was therefore of interest to find that under certain conditions these substances do have an inhibitory effect upon the action of pancreatic lipase. The data reported indicate that the monoesters of polyoxyethylene sorbitan with oleic, stearic, and lauric acid, commonly referred to as Tween 80,® 60,® and 20,® respectively, inhibit the action of pancreatic lipase upon corn oil *in vitro*. Since the "Tweens" are themselves digested by pancreatic lipase, but at a much slower rate, this may be an example of competitive inhibition in which a less reactive substrate inhibits enzyme action upon a more reactive substance.

This inhibition can be reversed by the addition of bile salts.—M. K. HORWITT

Effect of Emulsifiers on Fat Absorption in the Normal Young Adult. H. C. Tidwell and M. E. Nagler. *Gastroenterology* 23: 470, 1953.

No alterations in chylomicron curves or the areas beneath them were produced in 12 normal young men when ingested fat was supplemented with Tween 80® or glyceryl monoöleate.

The same substances when fed to rats as a 6 per cent supplement to a standard meal did not influence the rate of fat absorption as measured by recovery of the unabsorbed fat, fat splitting, or gastric or intestinal motility. The incidence of diarrhea, produced by the fatty diet, however (data excluded from study), was decreased in animals receiving Tween 80® or the monoglyceride.—S. H. LORBER

Normal Disappearance Curve of Emulsified Fat from the Blood Stream and Some Factors Which Influence It. W. R. Waddell, R. P. Geyer, I. M. Saslaw, and F. J. Stare. *Am. J. Physiol.* 174: 39, 1953.

The rate of disappearance of emulsified fat from the blood stream indicates a first order process except when gelatin was used. The emulsifying agents but not the chemical composition of the oil in the emulsion, influence the absolute rate of clearance of triglyceride oils.—M. J. OPPENHEIMER

Fat Absorption in Absence of Bile and Pancreatic Juice. V. C. Pessoa, K. S. Kim, and A. D. Ivy. *Am. J. Physiol.* 174: 209, 1953.

Endogenous lipid excretion was 39.4 mg./Kg. day in normal dogs, 142 in dogs with biliary fistulae, and 125 in those with pancreatic duct ligated. Triglycerides and fatty acids were absorbed better by normal dogs than by either of the operated groups. It was demonstrated that neither bile nor pancreatic juice is indispensable for absorption of any of the fats or fatty acids studied since 70 per cent of neutral fat and 55–75 per cent fatty acids were absorbed in their absence. Low melting-point unsaturated fatty acids are better absorbed than high melting-point saturated acids in dogs with pancreatic ducts ligated or, to a lesser extent, in those having a biliary fistula. This last observation is preliminary and requires further study. Normal dogs on a fat-free diet had twice as much endogenous fecal fat as soap as did those dogs having ligated pancreatic ducts or fistulae of the bile ducts. However, when corn oil was fed, biliary-fistula dogs showed twice as much as normal oil-fed dogs.—M. J. OPPENHEIMER

Even after fat is absorbed its metabolic fate is poorly understood. The circulation through the thoracic duct system is of obvious importance.

Removal of Intravenously Injected Fat from the Circulation and Its Appearance in the Thoracic Duct Lymph. H. C. Meng. *Am. J. Physiol.* 168: 335, 1952.

Intravenous fat injection was used to produce a hyperlipemia. Fat disappeared from the blood stream faster when the thoracic duct was ligated than when the thoracic duct was cannulated in the neck with or without saline replacement, or when it was cannulated in the chest or in control dogs. The output of lymph lipids was increased in all cannulated dogs although the concentration of lymph lipids was decreased and lymph flow increased. At best, intravenously injected fat could account for no more than 7 per cent of lymph fat. It is suggested that part of the injected fat leaves capillaries in liver, intestine, and adipose tissues to enter the thoracic duct by way of lymphatics. In this process fat is transformed and desaturated. The author points out that the lower serum total fatty acids when the thoracic duct is ligated might be explained by postulating an enzyme or hormone which accumulates under these conditions and has as its normal role removal of fat from the blood stream. Cannulation prevents the rapid removal of fat and supports this contention.—M. J. OPPENHEIMER

Investigation of the influence of irradiation upon the lipoprotein spectrum shows a correlation between increased lipoprotein levels and mortality of experimental animals.

Effect of Total Body Irradiation upon Lipoprotein. J. E. Hewitt, T. L. Hayes, J. W. Gofman, H. B. Jones, and F. T. Pierce. *Am. J. Physiol.* 172: 579, 1953.

These experiments demonstrated an excellent correlation between a high level of total lipoprotein thirty hours after irradiation and subsequent death of the animal. Low density lipoprotein is found with serum opalescence. This opalescence is not associated with total lipoprotein levels. It is pointed out

that radiation-produced changes in lipoprotein levels are compatible with the theory of conversion of low density lipoprotein to those of higher density. Return to normal levels of lipoprotein after exposure to radiation is hastened by heparin. On the other hand, toluidine blue produced changes in lipoprotein pattern which resembled those produced by irradiation. —M. J. OPPENHEIMER

Cholesterol remains the lipid-like substance of chief clinical interest. The effects of adenosine-5-monophosphate on lipids of experimental animals are briefly noted.

Effects of Adenosine-5-Monophosphate on Serum and Aortal Lipids in the Chicken. L. J. Milch, R. F. Redmond, W. W. Calhoun, H. I. Chinn, and the Cardiovascular Research Group. *Am. J. Physiol.* 170: 346, 1952.

When adenosine-5-monophosphate was given in low dose to six week-old cholesterol-fed cockerels there was a marked fall in total serum cholesterol and a smaller reduction in serum beta globulin. There was no change in the ratio of serum phospholipid to cholesterol. When large doses of adenosine-5-monophosphate were administered to atherosclerotic hens significant increases were produced in the phospholipid/cholesterol ratio, with but little change in the concentration of cholesterol in serum. The authors were of the opinion that there was a small increase in serum S_f 12–20 lipoprotein. Adenosine-5-monophosphate decreased fat and cholesterol concentration of atherosclerotic hen aortae. It is to be stressed that the effects on serum concentration of S_f 12–20 lipoproteins in atherosclerotic hens are not what might have been expected.—M. J. OPPENHEIMER

European experience with olive oil administered subcutaneously is recorded. Many questions, however, remain unanswered.

Parenteral Feeding with the Aid of Fat Infusions. W. Garn. *D. Ztschr. f. Verdauungs- u. Stoffwechselkrankheiten* 12: 113, 1952.

Parenteral fat, for the maintenance of the caloric requirement, is indicated in three groups of conditions: (1) when patients cannot be fed orally due to some mechanical interference; (2) when digestion and absorption have been impaired, and in cases where duodenal or peptic ulcers provoke vomiting; (3) when, on therapeutic grounds, avoidance of the oral route is desirable, as in certain types of ulcers (especially when bleeding) and in the period following operations in the gastrointestinal region. Supplementation of oral feeding is sometimes necessary, too, in cases of carcinoma, tuberculosis, nephritis, and particularly in loss of appetite in patients who have been confined to bed for long periods.

Parenteral fat has the advantage that more of it can be administered than by the oral route. However, it is practicable only for limited periods, since it can relieve only relative, not absolute, hunger. It may be advisable in some cases to supplement parenteral feeding with tube feeding by mouth or nose. (Opinion is still divided on the rectal absorption of food given by these various methods.)

Another characteristic of fat (as of other nitrogen-free substances) is its protein-sparing effect. With liberal feeding of carbohydrate and fat, nitrogen balance can be maintained on some 22–30 Gm. of protein daily.

Since the production of suitable fat emulsions for intravenous injection is attended with many difficulties, the author conducted several preliminary experiments with the subcutaneous method, which he considers simpler, safer, and more physiologic. Single injections of 40 cc. each of pure olive oil were given in the median area of the upper thigh. Up to as much as 200 cc. daily were administered. After the injections, the patients were permitted to walk about or, where this was impossible, active and passive exercises were prescribed to improve circulation and hence utilization of the oil. General tolerance was good. In 290 single injections, there were no instances of pain nor of infectious infiltrates. No tissue damage was observed. In one case, in which the patient succumbed to peritonitis, post-mortem investigation ruled out any possibility of fat embolism, and careful gross and microscopic examinations proved that the subcutaneously administered oil had been absorbed.

Four other patients, reduced by prolonged vomiting to a very poor state of health and nutrition, were given fat injections by the same method. In all 4 subjective and objective improvement was noted, and the acute caloric undernourishment was corrected. An interesting side effect of parenteral fat administration was the overall sedative effect reported by the author.—C.-J. HOWELL

The wartime restriction of dietary fats has been given credit for the reduction in coronary sclerosis encountered during these years. One wonders whether the lowered incidence of coronary artery disease could not be attributed to the reduction in the total caloric intake rather than to fat restriction alone.

The Connection between Nutrition and Mortality from Coronary Sclerosis during and after World War II. H. E. Schornagel. *Documenta Med. Geograph. Trop.* 5: 173, 1953.

Based on autopsy material from Rotterdam (The Netherlands), it was found there were considerably fewer deaths from coronary sclerosis during World War II than in the ensuing years of peace. Although the decrease in frequency during the war years was rather slow and gradual, the increase after the war was very rapid both in men and women. There is suggestive evidence that this is related to the nutritional intake and particularly to a diet rich in fat.—S. O. WAIFE

ITEMS OF GENERAL INTEREST

Identification of the Xanthine Oxidase Factor as Molybdenum. E. C. De Renzo, E. Kaleita, P. G. Heytler, J. J. Oleson, B. L. Hutchings, and J. H. Williams. *Arch. Biochem.* 45: 247, 1953.

Dietary factors like riboflavin and protein are known to influence the concentration of certain enzymes like xanthine oxidase in animal tissue. Westerfeld and Richert have shown that an unknown factor in natural materials increases the tissue level of xanthine oxidase in rats. This paper presents evidence to show that molybdenum is the xanthine oxidase factor. This is the first report of a role for molybdenum in animal nutrition and metabolism. The techniques used involve the assay of the xanthine oxidase of the intestines of rats fed on the basal diet plus various additives of liver residue. All compounds of molybdenum tested were active. These included ammonium molybdate, phosphomolybdic acid, molybdic acid, and sodium molybdate. The molybdenum compounds were highly specific since no other elements studied produced this enhancement of xanthine oxidase activity. The exact requirement of molybdenum was not determined with these experiments, but it must be very small. Diets containing 0.02 μg. of molybdenum per gram (50 μg. sodium molybdate dihydrate/Kg.) were sufficient to produce a "saturation level" of xanthine oxidase. The maximum daily requirement of the rat was calculated to be in the order of 0.2–0.3 μg. of molybdenum.—M. K. Horwitt

Effect of Strenuous Physical Activity on Blood Vitamin A and Carotene in Young Men. W. H. James and I. M. ElGindi. *Science* 118: 629, 1953.

Blood samples for vitamin A and carotene analyses were taken three minutes before the start of a 40–50 minute period of strenuous physical activity which included running five or six 220-yard dashes at full speed. Six minutes after the completion of the last dash, a second series of blood samples was taken. The average blood vitamin A level of a group of 12 subjects who performed these exercises increased an average of 43 per cent, with individual changes varying from an increase of 106 per cent to a decrease of 22 per cent. The average carotene level decreased 10 per cent, with individual changes varying from +17 to −50 per cent. It was stated that the subject whose vitamin A level increased to 106 per cent was in "poor condition," while the only runner to show a decrease in blood vitamin A was in "excellent condition."—M. K. Horwitt

Hypervitaminosis A: Report of a Case in an Adult Male. E. W. Shaw and J. Z. Niccoli. *Ann. Int. Med.* 39: 131, 1953.

This is an interesting case report of a condition apparently quite rare in adults but certainly worth thinking about in men, considering the widespread indiscriminate and abusive use of potent vitamin preparations. The presence of hypervitaminosis A was associated with anorexia, weight loss, asthenia, skin rash, loss of hair, polydypsia, polyuria, fissuring of the lips, bone and joint pain, hepatomegaly, tachycardia, and a peculiar pungent odor to a greasy skin. These symptoms and signs cleared promptly on mere withdrawal of the vitamin A. It is of interest that blood vitamin A levels were elevated several times normal, and there was a reciprocal depression of the blood carotene level.—J. F. Mueller

Preliminary Report on the Effect of Smoking on the Ascorbic Acid Content of Whole Blood. A. Bourquin and E. Musmanno. *Am. J. Dig. Dis.* 20: 75, 1953.

Observations were made on the effect of smoking on blood ascorbic acid levels. Although the results suggest that smoking decreases blood ascorbic acid content, too few observations were made to draw any conclusions.—S. H. Lorber

A Balance Sheet of the Estimation of Energy Intake and Energy Expenditure as Measured by Indirect Calorimetry, Using the Kofranyi-Michaelis Calorimeter. R. Passmore, J. G. Thomson, and G. M. Warnock. *Brit. J. Nutrition* 6: 253, 1952.

One method of assessing food requirements is the measurement of energy expended, in terms of heat loss, during various physical activities. The Kofranyi-Michaelis Calorimeter was used to estimate the energy expenditure of 5 subjects over a period of 13 days, during 5 of which the subjects carried out tasks involving great energy expenditure. The results were compared with the energy value of the food eaten during the same period. A satisfactory agreement between these two estimates over this comparatively short period was found, although 3 subjects were affected by the severity of the work involved in some of the tasks for which they were not in training. The authors suggest that the technique they employed might be used to estimate the energy expenditure of operatives, especially those engaged in heavy industry.—B. Sure

Caloric Requirement of Man in Cold Climates: Theoretical Considerations. A. P. Webster. *J. Applied Physiol* 4: 134, 1952.

This study furnishes basic equations for estimating heat needed to warm and humidify inspired air at various air temperatures, and for the fraction of the total energy metabolism involved in this process. From these equations and estimations of the heat necessary to warm and humidify inspired air, tables and graphs are shown for the increase in food intake or caloric requirement of man which might be expected in cold climates at various air temperatures. The author also provides hypothetical equations and calculations for the ratio of survival time without/with conversation of heat to warm and humidify inspired air.—M. J. Oppenheimer

Effect of Choline on Certain Forms of Edema. T. F. Bloem, and H. Neumann. *Lancet* 1: 827, 1953.

In two patients with edema, in one case due to starvation and in the other to nephrosis, choline chloride (3 Gm. daily by mouth) led to a rapid disappearance of the edema. The rationale for this treatment was the observation that during the famine in Holland in the last war, patients with hunger edema had a low blood level of lipid phosphorus. The daily rations contained small amounts of methionine, choline, and lecithin, and the authors believe that choline deficiency may be a factor in hunger edema.—S. O. WAIFE

Studies on the Effect of Intravenously Administered Choline Chloride in Patients with and without Liver Disease. F. Steigmann, R. Firestein, and J. de la Huerga. *Gastroenterology* 24: 44, 1953.

Choline chloride, equivalent to 2 grams of choline base, dissolved in 500 cc. of a 5 per cent glucose solution, was administered intravenously to 12 patients. No significant changes were observed in the blood pressure, pulse rate, blood picture, or urine. The electrocardiograms showed little change except in one case in which the P-R interval increased from 0.18 to 0.3 second. Mild side effects consisted of sensation of chilliness or warmth, headache, lightheadedness and dizziness. One patient had a shaking chill, but severe cholinergic effects were not observed. The authors believe that choline may be administered intravenously to humans with safety.—S. H. LORBER

Electrolyte Metabolism During Rice Diet. II. Serum Electrolytes in Patients with Severe Primary or Secondary Renal Disease. E. Peschel and R. L. Peschel. *Arch. Int. Med.* 91: 296, 1953.

This report is an evaluation of serum electrolyte concentrations in 80 patients with severe primary or secondary renal damage, who were maintained on a low sodium intake (rice diet). These patients had an average initial blood nonprotein nitrogen of 77 mg. per 100 cc., and an average PSP excretion of 22 per cent in two hours. Surprisingly, a high percentage of these patients showed no disturbance in electrolyte concentration. In those who did, tiny amounts of sodium replacement were sufficient to return the serum electrolyte levels to normal.—L. W. KINSELL

The Management of Intractable Sprue, with Cortisone and Adrenal Corticotropin. H. Colcher, S. R. Drachman, and D. Adlersburg. *Ann. Int. Med.* 38: 554, 1953.

Eight patients with a sprue syndrome unresponsive to the usual high protein, low fat diet, crude or refined liver extract, folic acid and vitamin B_{12}, calcium, multiple vitamin preparations, vitamin K, Tween 80®, pancreatin, bile salts, multiple plasma and blood transfusions, and oral antibiotics, were treated with steroid therapy. These patients had mild anemia, slight macrocytosis, hypoprothrombinemia, hypoalbuminemia, hypocalcemia, flat vitamin A and glucose tolerance tests. All but one showed the characteristic deficiency pattern in the small intestines on roentgenological examination. ACTH (corticotropin) was administered in doses of 25 mg. 4 times a day intramuscularly, followed by cortisone 100 mg. daily in divided doses after the patients left the hospital. Previous therapy was usually continued until a remission was induced. Edema occurred in some patients. Several developed abscesses at the sites of injection but these were easily controlled.

Clinical remissions were observed in all patients. The diarrhea disappeared and fat usually decreased in the stool. There was an increased sense of well being and an improvement in appetite and body weight. In some instances improvement was noted in the serum albumin, the serum calcium, and the roentgenologic findings in the small intestine. Relapse occurred within five weeks after cessation of hormonal therapy but a clinical remission occurred when this therapy was begun again. Twenty-five to 50 mg. of cortisone a day sometimes was sufficient to maintain the patients in remission. These data indicate that the steroids influence intestinal absorption and offer a potent therapeutic tool in the control of an otherwise intractable sprue syndrome.—R. W. VILTER

Factors Influencing the Response of Adrenalectomized Rats' Distress. M. E. Dumm and E. P. Ralli. *Metabolism* 2: 153, 1953.

The role of certain nutritional factors in their reaction to stress was studied in young rats by means of the length of time such animals can swim in cool water. It was found that pantothenate increased the swimming time of rats when given as a dietary supplement. The ability to sustain swimming was also increased by the addition to the diet of large doses of folic acid or biotin, but not to the same extent as when the pantothenate content was increased. Conversely, a deficiency of pantothenate impaired the ability of the rats to sustain the stress. It is interesting that swimming, which is a severe stress for an adrenalectomized animal, was not impaired when a high intake of calcium pantothenate was administered to adrenalectomized rats. Thus the authors correctly conclude that the responses of both intact and adrenalectomized rat stress can be influenced by nutritional factors.—S. O. WAIFE

Skim Milk Powders and Experimental Rat Caries. F. J. McClure and J. E. Folk. *Proc. Soc. Exper. Biol. & Med.* 83: 21, 1953.

In previous studies, the authors had shown that heat processing of cereal foods predisposed toward a type of dental caries in the rat. Rats receiving diets in which the major source of protein was skim milk had a significantly higher incidence of surface caries when the skim milk was heat treated. Certain other factors in the processing of skim milk may also play a part in its cariogenic activity.—L. W. KINSELL

Alterations of Intestinal Absorption in Ulcerative Colitis and in Intestinal Hypermotility; Modification of these Alterations in Ulcerative Colitis by Tween 80, ACTH and Cortisone. K. Uyeyama, J. E. Gianseracusa, T. L. Althausen, and H. A. Harper. *Gastroenterology* 23: 143, 1953.

Intestinal absorption in patients with ulcerative colitis and functional hypermotility of the small intestine was studied by administering vitamin A, galactose, and methionine orally and then determining the plasma concentrations of these substances at fixed intervals. In ulcerative colitis, reduced absorption of vitamin A and methionine was observed, but the absorption of galactose was increased. In small intestinal functional hypermotility, absorption of vitamin A and methionine was normal, but absorption of galactose was increased. Tween 80® did not modify, in consistent fashion, the vitamin A tolerance curves in patients with ulcerative colitis, but improvement was observed after administration of ACTH or cortisone. Although many metabolic factors other than absorption effect blood levels of ingested substances, the results observed are in keeping with the findings of others.—S. H. LORBER

Nutrition Following Total Gastrectomy, with Particular Reference to Fat and Protein Assimilation, a Collective Review. T. C. Everson. *Surg. Gynec. & Obst.* (*Intern. Abstr. Surg.*) 95: 209, 1952.

The literature concerning nutrition following total gastrectomy is reviewed. The available clinical and laboratory evidences indicate that there frequently is impairment of the assimilation of fat and protein following total gastrectomy. Only three of 40 patients in a collected series of cases had their weight restored to the preoperative level following total gastrectomy. The blood findings in 46 cases reported in the literature in which the patients had survived total gastrectomy for three years or more, indicate that 12 patients had findings resembling those of pernicious anemia, while in five patients the findings were of doubtful nature.

Possible factors responsible for the impairment of fat and protein assimilation after total gastrectomy are discussed as follows: (1) loss of digestive function of stomach; (2) loss of titurating function of the stomach; (3) decreased stimulation of pancreatic and biliary secretions; (4) improper or inadequate mixing of food with pancreatic and biliary secretion; (5) increased intestinal motility; and (6) loss of the reservoir function of the stomach.

In attempts to improve protein and fat assimilation after total gastrectomy, the author believes the following items should be considered: (1) esophagoduodenostomy versus esophagojejunostomy; (2) the use of oral pancreatic enzymes; (3) drugs which inhibit intestinal motility, such as atropine, Banthine®, and hexamethonium bromide; (4) the use of jejunal and colonic pouches; (5) adaptation with time; (6) diet and frequency of feeding; (7) "Tween-80,"® an emulsifying agent; (8) bile substitutes; and (9) miscellaneous agents such as hydrochloric acid, liver extract, lipocaic, stomach extract, and the vitamins A, D, and B_{12}.

In conclusion, the author states that there is no known drug nor any surgical procedure that will restore fat and protein assimilation to normal following total gastrectomy.

He emphasizes that it is most important for these patients to have a high caloric intake, that their food be well masticated, that they take small frequent feedings, and that fluids be limited at meal time. It is suggested that the patient have at least 50 calories per kilogram of body weight and that he receive from 200–250 Gm. of fat, 100–150 Gm. of protein, and 200–250 Gm. of carbohydrate daily. If the patient fails to maintain or regain his previous weight, then obviously he is not taking enough in the way of caloric intake. The diarrhea which occurs after total gastrectomy on occasion will respond to dilute hydrochloric acid, pancreatin, paregoric, or smaller meals. Vitamin and mineral supplements can be reserved for the patient who develops deficiency symptoms.—H. A. ZINTEL

Nicotinic Acid in the Treatment of Depression. W. L. Tonge. *Ann. Int. Med.* 38: 551, 1953.

A preliminary report by Washburn (*Ann. Int. Med.* 32: 261, 1950) suggested that patients with various forms of depression improved when treated with nicotinic acid. A series of 16 patients who were consecutive referrals to the University Clinic in Manchester, England were treated in a similar fashion to check these results. Nicotinic acid was given orally in total doses of 450 to 600 mg. for the first week and 900 mg. daily for two weeks. An inert tablet was used as a placebo. Of nine patients treated in the hospital in this fashion, improvement was noted in two who received nicotinic acid and two who received the placebo. Of the seven patients treated on an outpatient basis, two who received nicotinic acid improved. None were treated with placebo in this group. Although this is a very small series, particularly small in respect to placebo-treated patients, it suggests that the previous report referred to above was more enthusiastic than the material warranted. Since there is no evidence for decreased cerebral blood flow in the various types of depression, it is unlikely that a cerebral vasodilator would have any effect on the basic psychological pattern except through suggestion, and the flush which patients experience from nicotinic acid may be a very potent means of suggestion.—R. W. VILTER

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